Counts, G.
09/928048


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     FILE 'REGISTRY' ENTERED AT 09:43:09 ON 12 AUG 2003
=> e "cyclase-inhibiting parathyroid"/cn 5
E1            1     CYCLASE-GLUTAMINE AMIDOTRANSFERASE (ASPERGILLUS NIDULA
                    NS STRAIN A234 GENE HISHF)/CN
E2            1     CYCLASE-GLUTAMINE AMIDOTRANSFERASE (SACCHAROMYCES CERE
                    VISIAE STRAIN S288C CONGENIC GENE HIS7)/CN
E3            0 --> CYCLASE-INHIBITING PARATHYROID/CN
E4            1     CYCLASE-LIKE PROTEIN (STREPTOMYCES ARGILLACEUS STRAIN
                    ATCC-12956 GENE MTMX)/CN
E5            1     CYCLASE-LIKE PROTEIN (STREPTOMYCES ARGILLACEUS STRAIN
                    ATCC-12956 GENE MTMY)/CN

=> e "cyclase-inactivating parathyroid"/cn 5
E1            1     CYCLASE-GLUTAMINE AMIDOTRANSFERASE (ASPERGILLUS NIDULA
                    NS STRAIN A234 GENE HISHF)/CN
E2            1     CYCLASE-GLUTAMINE AMIDOTRANSFERASE (SACCHAROMYCES CERE
                    VISIAE STRAIN S288C CONGENIC GENE HIS7)/CN
E3            0 --> CYCLASE-INACTIVATING PARATHYROID/CN
E4            1     CYCLASE-LIKE PROTEIN (STREPTOMYCES ARGILLACEUS STRAIN
                    ATCC-12956 GENE MTMX)/CN
E5            1     CYCLASE-LIKE PROTEIN (STREPTOMYCES ARGILLACEUS STRAIN
                    ATCC-12956 GENE MTMY)/CN

=> e "cyclase inactivating parathyroid"/cn 5
E1            1     CYCLASE II (STREPTOMYCES AVERMITILIS STRAIN ATCC31267)
                    /CN
E2            1     CYCLASE II (STREPTOMYCES AVERMITILIS STRAIN MA-4680 GE
                    NE SPPE)/CN
E3            0 --> CYCLASE INACTIVATING PARATHYROID/CN
E4            1     CYCLASE RELATED PROTEIN (PYROCOCCUS ABYSSI STRAIN ORSA
                    Y)/CN
E5            1     CYCLASE SCIF3.09C (STREPTOMYCES COELICOLOR STRAIN A3(2
                    ) GENE SCIF3.09C)/CN

=> e "cyclase inhibiting parathyroid"/cn 5
E1            1     CYCLASE II (STREPTOMYCES AVERMITILIS STRAIN ATCC31267)
                    /CN
E2            1     CYCLASE II (STREPTOMYCES AVERMITILIS STRAIN MA-4680 GE
                    NE SPPE)/CN
E3            0 --> CYCLASE INHIBITING PARATHYROID/CN
E4            1     CYCLASE RELATED PROTEIN (PYROCOCCUS ABYSSI STRAIN ORSA
                    Y)/CN
E5            1     CYCLASE SCIF3.09C (STREPTOMYCES COELICOLOR STRAIN A3(2
                    ) GENE SCIF3.09C)/CN
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     FILE 'REGISTRY' ENTERED AT 15:42:16 ON 12 AUG 2003
L1           747 S CYCLASE?/CN
                 E PARATHYROID HORMONE/CN
L2            12 S E3-E13
                 E PARATHORMONE/CN
L3            10 S E3 OR E4 OR E6 OR E8-E10 OR E13 OR E15 OR E16
L4            20 S L2 OR L3

     FILE 'HCAPLUS' ENTERED AT 15:43:08 ON 12 AUG 2003
L1           747 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLASE?/CN
L2            12 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("PARATHYROID HORMONE"/
                 CN OR "PARATHYROID HORMONE (BOVINE)"/CN OR "PARATHYROID
                 HORMONE (HUMAN)"/CN OR "PARATHYROID HORMONE (HUMAN)
                 FUSION PROTEIN WITH APELIN 36 (HUMAN)"/CN OR "PARATHYROID
                  HORMONE (HUMAN) FUSION PROTEIN WITH G PROTEIN-COUPLED
                 RECEPTOR 8 GPR8 LIGAND (HUMAN)"/CN OR "PARATHYROID
                 HORMONE (HUMAN) FUSION PROTEIN WITH G PROTEIN-COUPLED
                 RECEPTOR ZAQ LIGAND (HUMAN)"/CN OR "PARATHYROID HORMONE
                 (MACAQUE)"/CN OR "PARATHYROID HORMONE (PORCINE)"/CN OR
                 "PARATHYROID HORMONE (RAT)"/CN OR "PARATHYROID HORMONE
                 (RATTUS NORVEGICUS 115-AMINO ACID)"/CN OR "PARATHYROID
                 HORMONE (SYNTHETIC CLONE 4PTH)"/CN)
L3            10 SEA FILE=REGISTRY ABB=ON  PLU=ON  PARATHORMONE/CN OR
                 "PARATHORMONE (16-ASPARTIC ACID) (HUMAN)"/CN OR "PARATHOR
                 MONE (29-HISTIDINE) (HUMAN)"/CN OR ("PARATHORMONE
                 (35-CYSTEINE) (HUMAN)"/CN OR "PARATHORMONE (37-THREONINE)
                  (HUMAN)"/CN OR "PARATHORMONE (57-ASPARTIC ACID)
                 (HUMAN)"/CN) OR "PARATHORMONE (8-CYSTEINE) (HUMAN)"/CN
                 OR "PARATHORMONE (CANIS FAMILIARIS)"/CN OR "PARATHORMONE
                 (CATTLE)"/CN
L4            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L3
L5         44180 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR CYCLASE
L6         18634 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR (PARATHYROID? OR
                 PARA THYROID?)(W)HORMONE OR PARATHORMONE OR PTH
L7          1285 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5(L)L6
L8           531 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7(L)(INHIBIT? OR
                 INACTIVAT?)
L9            27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND ANTIBOD?

L9   ANSWER 1 OF 27  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:548789  HCAPLUS
DOCUMENT NUMBER:          139:79534
TITLE:                    Procedure and devices for direct determination
                          of cyclase-inhibiting
                          parathormone
INVENTOR(S):              Cantor, Thomas L.
PATENT ASSIGNEE(S):       Scantibodies Laboratory, Inc., USA
SOURCE:                   Ger. Offen., 10 pp.
                          CODEN: GWXXBX
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     DE 10236631        A1   20030717      DE 2002-10236631 20020809
     US 2003138858      A1   20030724      US 2001-928048   20010810
```

PRIORITY APPLN. INFO.: US 2001-928048 A 20010810
US 2000-224447P P 20000810

AB The present invention concerns new procedures and devices for direct detn. of presence or quantity of **cyclase-inhibiting parathormone** which is present in a clin. sample. Such detns. are useful, in order to differentiate parathyroidal illnesses such as hyperparathyroidism from normal conditions or the condition of not being sick. The target analyte is a large, incomplete **parathormone** peptide fragment, which can function as a **cyclase**-activating **parathormone** antagonist.

IT **9002-64-6, Parathormone**
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(direct detn. of **cyclase-inhibiting parathormone** in human clin. samples)

IT **9074-90-2, Cyclase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; direct detn. of **cyclase-inhibiting parathormone** in human clin. samples)

L9 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:42075 HCAPLUS
DOCUMENT NUMBER: 138:88657
TITLE: Preparation and application of **antibodies** to human parathyroid hormone
INVENTOR(S): Hutchison, James Scott
PATENT ASSIGNEE(S): Quest Diagnostics Investments Incorporated, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003003986	A2	20030116	WO 2002-US21356	20020703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003082179	A1	20030501	US 2001-898398	20010703

PRIORITY APPLN. INFO.: US 2001-898398 A 20010703

AB The author discloses the prepn. of **antibodies** that recognize and bind to three-dimensional epitopes in the N-terminus of human parathyroid hormone (PTH). The **antibodies** are used in diagnostic and therapeutic applications.

IT **9012-42-4**, Adenylate **cyclase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activation by human **parathyroid hormone** is **inhibited** by anti-**PTH antibodies**)

L9 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:274743 HCAPLUS
DOCUMENT NUMBER: 134:339129
TITLE: Endogenous prostaglandin E2 and insulin-like growth factor 1 can modulate the levels of parathyroid hormone receptor in human osteoarthritic osteoblasts
AUTHOR(S): Hilal, George; Massicotte, Frederic; Martel-Pelletier, Johanne; Fernandes, Julio C.; Pelletier, Jean-Pierre; Lajeunesse, Daniel
CORPORATE SOURCE: Osteoarthritis Research Unit, Hopital Notre-Dame, Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Can.
SOURCE: Journal of Bone and Mineral Research (2001), 16(4), 713-721
CODEN: JBMREJ; ISSN: 0884-0431
PUBLISHER: American Society for Bone and Mineral Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Subchondral bone sclerosis may be important for the onset and/or progression of cartilage loss/damage in human osteoarthritis (OA). OA osteoblasts are resistant to parathyroid hormone (PTH) stimulation, which could explain bone sclerosis via the inhibition of PTH-dependent catabolism. Here, the authors investigated the mol. mechanism(s) responsible for reduced PTH-dependent cAMP synthesis in OA subchondral osteoblasts. Although cholera toxin (CTX) increased basal cAMP formation in these cells, it failed to stimulate PTH-dependent cAMP synthesis, whereas pertussis toxin (PTX) did not inhibit basal cAMP, yet diminished PTH-dependent cAMP prodn. Binding of 125I-PTH indicated lower PTH receptor levels in OA than in normal osteoblasts (-50.5%). This could be attributed to either reduced expression of the PTH receptor (PTH-R) or altered recycling of existing pools of receptors. Reverse-transcription polymerase chain reaction (RT-PCR) anal. indicated decreased PTH-R mRNA levels in OA cells that were highly variable (ranging from -10% to -60%), a situation that reflects disease severity. Interestingly, OA osteoblasts produced more prostaglandin E2 (PGE2) than normal osteoblasts, and using naproxen, a cyclo-oxygenase inhibitor, increased PTH-dependent cAMP formation to a level similar to normal osteoblasts. Because heterologous desensitization can explain a decrease in PTH binding but cannot account for reduced PTH-R expression, the authors looked at the possible effect of insulin-like growth factor 1 (IGF-1) on this parameter. Blocking IGF-1 signaling with a neutralizing receptor **antibody** increased 125I-PTH binding in both normal and OA osteoblasts. Conversely, treatments with IGF-1 receptor (IGF-1R) **antibody** only slightly increased the levels of PTH-R mRNA, whereas the addn. of IGF-1 significantly reduced PTH-R mRNA levels (-24.1%), yet neither PGE2 nor naproxen modified PTH-R levels. These results suggest that both IGF-1 signaling and PGE2 formation repress PTH-dependent response in OA osteoblasts, a situation that can contribute to abnormal bone remodeling and bone sclerosis in OA.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:211002 HCAPLUS
DOCUMENT NUMBER: 132:232198
TITLE: Effects of calcium-related peptide hormones on cAMP in cultured dental pulp cells of the rabbit
AUTHOR(S): Saitoh, Kouichi
CORPORATE SOURCE: Biosignal Res. Cent., Inst. Mol. Cell. Regul., Gunma Univ., Maebashi, 371-8512, Japan
SOURCE: Kitakanto Medical Journal (2000), 50(2), 83-92
CODEN: KMJOFG; ISSN: 1343-2826
PUBLISHER: Kitakanto Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB **Parathyroid hormone** (**PTH**) and calcitonin (CT) are known to affect not only bone tissue but also dentin tissue. In the mechanism of action of these hormones on bone tissue, involvement of adenylate **cyclase**-cAMP system has been reported. However, studies of the mechanism of these hormones on dentin tissue remain insufficient. Using TCA extn. and double **antibody** RIA, the content of cAMP in dentin pulp tissue was shown to be much higher than that in the serum. Using dental pulp cells obtained from rabbits of 600 g body wt. and cultured for 4 days, which abounded in odontoblasts, cAMP levels in the culture media after 30 min' contact with hormones were examd. **PTH**, at 0.01-1.0 .mu.M, increased cAMP levels significantly in a concn.-dependent manner. CT and parotin, on the other hand, did not influence cAMP levels when added sep. However, when **PTH** (1 .mu.M) and CT (10 .mu.M) were added together, the increase of extracellular cAMP caused by **PTH** was **inhibited** by about 50%, indicating a possible interaction of these hormones in the signal transduction in the odontoblasts.

L9 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:46238 HCAPLUS
DOCUMENT NUMBER: 132:161543
TITLE: Parathyroid hormone-related peptide stimulates DNA synthesis and insulin secretion in pancreatic islets
AUTHOR(S): Villanueva-Penacarrillo, M. L.; Cancelas, J.; De Miguel, F.; Redondo, A.; Valin, A.; Valverde, I.; Esbrit, P.
CORPORATE SOURCE: Department of Metabolism, Nutrition and Hormones, Madrid, Spain
SOURCE: Journal of Endocrinology (1999), 163(3), 403-408
CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Parathyroid hormone** (**PTH**)-related protein (PTHrP) is present in the pancreatic islet. Recent data in transgenic mice suggest that PTHrP might modulate islet mass and insulin secretion. In the present study, the authors assessed the effect of the N-terminal **PTH**-like region of PTHrP on DNA synthesis in isolated rat islets. PTHrP (1-34), between 1 pM and 10 nM, for 48 h stimulated [3H]thymidine incorporation into rat islets. This effect was maximally induced, about 2.5-fold over control, by 10 pM of this peptide, decreasing thereafter. In contrast, PTHrP (38-64) amide or PTHrP (107-139) were ineffective in increasing DNA synthesis in islets. Using reverse transcription followed by PCR,

the authors confirmed that rat islets express PTHrP and the type 1 **PTH**/PTHrP receptor. Addn. of a neutralizing anti-PTHrP **antibody** to the incubation medium of proliferating islets decreased islet DNA synthesis by 30%. The effect of a submaximal dose (30 pM) of PTHrP (1-34) on DNA synthesis in rat islets was abolished by 25 nM bisindolylmaleimide I, a protein kinase C (PKC) **inhibitor**, but not by 25 .mu.M adenosine 3',5'-cyclic monophosphorothioate, Rp-isomer, a protein kinase A **inhibitor**. Moreover, 100 nM phorbol-12-myristate-13-acetate for 48 h also increased DNA synthesis 2-fold over controls in islets. PTHrP (1-34), at 100 nM, in contrast to 50 .mu.M forskolin or 10 mM NaF, failed to affect adenylate **cyclase** activity in islet membranes. PTHrP, at 30 pM, was also found to increase 2-fold insulin released into the islet-conditioned medium within 24-48 h. The authors' results suggest that PTHrP is a modulator of pancreatic islet growth and/or function by a PKC-mediated mechanism.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:221660 HCAPLUS
DOCUMENT NUMBER: 126:304503
TITLE: Renal dopamine DA1 receptor coupling with Gs and Gq/11 proteins in spontaneously hypertensive rats
AUTHOR(S): Hussain, Tahir; Lokhandwala, Mustafa F.
CORPORATE SOURCE: Coll. Pharm., Univ. Houston, Houston, TX, 77204-5511, USA
SOURCE: American Journal of Physiology (1997), 272(3, Pt. 2), F339-F346
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The dopamine DA1 receptor transduces its signal via adenylyl **cyclase** and phospholipase C in the renal proximal tubule, which has been suggested to be defective at the level of receptor-G protein coupling in spontaneously hypertensive rats (SHR). The authors prepd. basolateral membranes from Wistar-Kyoto (WKY) rats and SHR to det. the coupling of DA1receptor with G proteins, esp. Gq/11. Fenoldopam, a DA1-receptor agonist, produced a time- and concn.-dependent stimulation in 35S-labeled guanosine 5'-O-(3-thiotriphosphate) ([35S]GTP.gamma.S) binding in WKY rats. Fenoldopam-induced (10 .mu.M) stimulation was significantly **inhibited** by a DA1-receptor antagonist, Sch-23390. Specific **antibodies** against COOH terminals of Gs.alpha. and Gq/11.alpha. produced 50-60% and 40-50% **inhibition**, resp., in fenoldopam stimulation of [35S]GTP.gamma.S binding. Western anal. of basolateral membranes with these **antibodies** revealed the presence of Gs.alpha. (45 kDa) and Gq/11.alpha. (42 kDa). Fenoldopam stimulation of [35S]GTP.gamma.S binding was significantly attenuated in SHR compared with WKY rats. **Parathyroid hormone** stimulation of [35S]GTP.gamma.S binding was similar in SHR and WKY rats, whereas stimulation by phenylephrine was significantly reduced in SHR. Densitometric quantification of 42-kDa band showed a reduced amt. in SHR, whereas the d. of 45-kDa band was not significantly different

compared with WKY rats. The authors provide the direct evidence showing the coupling of DA1 receptor with Gq/11.alpha. and Gs.alpha. and propose that, in addn. to a defect in the receptor-G protein coupling, a reduced amt. of Gq/11.alpha. obsd. in the hypertensive animals may also contribute to the diminished dopamine-induced **inhibition** of Na+-K+-ATPase in SHR.

L9 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:92679 HCAPLUS
DOCUMENT NUMBER: 126:181661
TITLE: Multiple G-protein involvement in parathyroid hormone regulation of acid production by osteoclasts
AUTHOR(S): May, Lisa G.; Gay, Carol V.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, The Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Journal of Cellular Biochemistry (1997), 64(1), 161-170
CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The involvement of multiple G-proteins in parathyroid hormone regulation of acid prodn. was demonstrated in a highly enriched osteoclast population. Osteoclasts were isolated from the endosteum of 2.5 to 3-wk-old chicken tibia using sequential enzymic digestion. Single cell anal. of acid prodn. was accomplished using microscope photometry and vital staining with acridine orange, a hydrogen ion concn. sensitive fluorescent dye. Lithium chloride, an uncoupler of G-proteins from their resp. receptors, blocked parathyroid hormone stimulated prodn. of acid. Cholera toxin, which permanently activates Gs-proteins, mimicked PTH stimulation. Pertussis toxin, which prevents receptor interaction with Gi- and Go-proteins, blocked both 10-8 M and 10-11 M PTH stimulated acid prodn., suggesting that the pertussis toxin-sensitive G-protein is utilized at both PTH concns. Immunoblots of osteoclast plasma membrane proteins, using a panel of **antibodies** generated against specific G-protein .alpha. subunits, revealed a 48 kDa Gs.alpha., a 41 kDa Go.alpha., a 34 kDa Gi.alpha.-3, and a unique 68 kDa G.alpha. subunit, with the 41 kDa and 34 kDa bands being the most intense. Immunoblots of osteoblast plasma membrane proteins had a substantially different profile with the most intense bands being a Gs.alpha. (48 kDa) and a Go.alpha. (36 and 38 kDa). The studies suggest the utilization of at least two different G-proteins in the parathyroid hormone regulation of acid formation by osteoclasts, a Gs and a pertussis toxin-sensitive G-protein (Go and/or Gi.alpha.-3).

L9 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:84531 HCAPLUS
DOCUMENT NUMBER: 126:127199
TITLE: Parathyroid hormone-related protein (PTHrP) - a paracrine factor in astrocytes and an autocrine factor in astrocytomas
AUTHOR(S): Turzynski, A.; Struckhoff, G.; Colangelo, D.; Guidotto, S.; Bunge, A.; Dietel, M.
CORPORATE SOURCE: Institut fur Pathologie der charite,

Humboldt-Universitat, Berlin, D-24098, Germany
SOURCE: Peptidergic Neuron, [International Symposium on Neurosecretion] 12th, Kiel, Sept. 20-22, 1995 (1996), Meeting Date 1995, 343-351. Editor(s): Krisch, Brigitte; Mentlein, Rolf. Birkhaeuser: Basel, Switz.
CODEN: 63XVA3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB **Parathyroid hormone**-related protein (PTHrP), that has been identified as the main causative factor for the humoral hypercalcemia of malignancy, is nearly ubiquitously expressed in tumors and normal tissues of various histogenesis. In normal tissues as well as in malignant conditions as auto- or paracrine function as growth and differentiation factor has been demonstrated. In cultured astrocytes of the rat brain we found an expression of the **PTH**/PTHrP receptor. Since normal astrocytes in situ and in vitro fail to express PTHrP by themselves, they presumably represent the physiol. target for meningeal PTHrP via a paracrine mechanism. In normal astrocytes PTHrP induces an activation of adenyl **cyclase** accompanied by glial stellation, an effect possibly involved in the formation of the glial limiting membrane. Surprisingly, in the majority of the astrocytomas (grade II - grade IV, WHO-classification) PTHrP immunoreactivity can be detected. To test the biol. significance of this observation we simultaneously performed the reverse transcription polymerase chain reaction for PTHrP and **PTH** /PTHrP receptor mRNA in three astrocytoma cell lines. In all three astrocytomas investigated the specific amplification products were detected, thus, indicating a possible autocrine function of PTHrP. In the monolayer proliferation assay the application of a monoclonal PTHrP-**antibody** against the receptor-binding N-terminus **inhibited** the proliferation of two astrocytoma cell lines, esp. when they were selected at low cell densities. Accordingly, in the clonogenic assay both cell lines showed a marked redn. in their ability to form clones. The data indicate a functional shift of PTHrP from a paracrine to an autocrine mode, occurring during the development of the astrocytomas. The simultaneous expression of PTHrP and its receptor and the effect on the proliferation in vitro substantiate its role as a growth factor in astrocytomas.

L9 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:668561 HCAPLUS
DOCUMENT NUMBER: 125:318217
TITLE: Parathyroid hormone-related protein detection and interaction with NO and cyclic AMP in the renovascular system
AUTHOR(S): Massfelder, Thierry; Stewart, Andrew F.; Endlich, Karlhans; Soifer, Neil; Judes, Clement; Helwig, Jean-Jacques
CORPORATE SOURCE: Lab. Physiol. Cell. Renale, Univ. Louis Pasteur, Strasbourg, Fr.
SOURCE: Kidney International (1996), 50(5), 1591-1603
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The presence of **parathyroid hormone**-related

protein (PTHrP) in human kidney vasculature and the signal transduction pathways stimulated during PTHrP-induced vasodilation of the rabbit kidney were investigated. Immunostaining of human kidney revealed the abundant presence of PTHrP in media and intima of all microvessels as well as in macula densa. In isolated perfused rabbit kidney preconstricted with noradrenaline, 10-5 M Rp-cAMPS, a direct **inhibitor** of protein kinase A, produced comparable **inhibition** of 2.5 .times. 10-7 M forskolin- and 10-7 M PTHrP-induced vasorelaxations. Renal vasorelaxation and renal microvessel adenylyl **cyclase** stimulation underwent comparable desensitization following exposure to PTHrP. Nitric oxide (NO)-synthase **inhibition** by L-NAME (10-4 M), NO scavenging by an imidazolineoxyl N-oxide (10-4 M) decreased PTHrP-induced vasorelaxation by 27 to 53%, abolished bradykinin-induced vasorelaxation and did not affect forskolin-induced vasorelaxation. The effects of Rp-cAMPS and L-NAME were not additive on PTHrP-induced vasorelaxation. Damaging endothelium by treating the kidney with either anti-factor VIII-related **antibody** and complement, gossypol or detergent, did not affect PTHrP- or forskolin-induced vasorelaxations but reduced bradykinin-induced vasorelaxation by 53 to 92%. Conversely, endothelial damage did not alter the **inhibitory** action of L-NAME on PTHrP-induced vasorelaxation. In conclusion, PTHrP is present throughout the human renovascular tree and juxtaglomerular app. Activation of both adenylyl **cyclase**/protein kinase A and NO-synthase/guanylyl **cyclase** pathways are directly linked to the renodilatory action of PTHrP in a way that does not require an intact endothelium in the isolated rabbit kidney.

L9 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:496184 HCAPLUS
DOCUMENT NUMBER: 125:159099
TITLE: Regulation of the renal Na-HCO3 cotransporter: V. Mechanism of the inhibitory effect of parathyroid hormone
AUTHOR(S): Ruiz, Ofelia S.; Qiu, Yi-Yong; Wang, Long-Jiang; Arruda, Jose A.L.
CORPORATE SOURCE: Section of Nephrology, University of Illinois, Chicago, IL, USA
SOURCE: Kidney International (1996), 49(2), 396-402
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **PTH** administration decreases proximal HCO3 resorption and **inhibits** the brush border Na-H antiporter. The authors studied the effect of **PTH** on the renal Na-HCO3 cotransporter and examd. whether this effect is mediated through the adenylate **cyclase**/cAMP system or through the phospholipase A pathway. The authors studied the effect of **PTH** [1-34] on the Na-HCO3 cotransporter activity in rabbit renal basolateral membranes incubated with 50 .mu.M ATP by measuring the 22Na uptake in the presence of HCO3 and gluconate. Na-HCO3 cotransporter activity (expressed in nmol/mg protein/3 s) was taken as the difference in 22Na uptake in the presence of HCO3 and gluconate. **PTH** (10-10 M) completely **inhibited** Na-HCO3 cotransporter activity from 1.23 to -0.58,.. This effect of

PTH to **inhibit** the Na-HCO3 cotransporter was prevented by the polyclonal **antibody** against G.alpha.s indicating that **PTH** acts through G.alpha.s protein. Because G.alpha.s stimulates adenylate **cyclase**/cAMP system, the authors examd. the effect of **PTH** in the presence and in the absence of the adenylate **cyclase inhibitor**, dideoxyadenosine (DDA). DDA alone (10-4 M) stimulated the Na-HCO3 cotransporter activity. In the presence of DDA, the net **inhibitory** effect of **PTH** was the same magnitude as that of control, suggesting the existence of other pathways for the effect of **PTH** on the cotransporter. Calmodulin **inhibition** also partially prevented the effect of **PTH**. To det. whether the **inhibitory** effect of **PTH** is mediated at least in part, through phospholipase A, the authors first examd. the effect of **PTH** on arachidonic acid release and then measured the Na-HCO3 cotransporter activity in presence and in absence of arachidonic acid or eicosatetraynoic acid (ETA), an **inhibitor** of arachidonic acid metab. **PTH** significantly increased the release of arachidonic acid by isolated proximal tubule cells and arachidonic acid **inhibited** the Na-HCO3 cotransporter in basolateral membranes. ETA (3 .mu.M) partially prevented the **inhibitory** effect of **PTH**. In cultured proximal tubule cells, **PTH inhibited** the HCO3-dependent 22Na uptake and ethoxyresorufin, an **inhibitor** of cytochrome P 450, blocked the **inhibitory** effect of **PTH** on the cotransporter. These results demonstrate that **PTH inhibits** the renal Na-HCO3 cotransporter through multiple mechanisms, that are mediated through G proteins, G.alpha.s and Gp, and CaM-KII.

IT **9012-42-4**, Adenylate **cyclase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mechanism of the **inhibitory** effect of **parathyroid hormone** in the regulation of the renal Na-HCO3 cotransporter)

L9 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:821586 HCAPLUS
DOCUMENT NUMBER: 123:218903
TITLE: Agonist-stimulated phosphorylation of the G protein-coupled receptor for parathyroid hormone (PTH) and PTH-related protein
AUTHOR(S): Blind, Eberhard; Bambino, Tom; Nissenson, Robert A.
CORPORATE SOURCE: Endocrine Unit, Univ. California, San Francisco, CA, 94121, USA
SOURCE: Endocrinology (1995), 136(10), 4271-7
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objectives of the present study were to det. whether the G protein-coupled receptor for **PTH** and **PTH**-related protein (PTHrP) is subject to agonist-specific phosphorylation and to characterize the relevant kinase(s). The opossum kidney **PTH**/PTHrP receptor stably expressed in human embryonic kidney 293 cells was coupled to adenylyl **cyclase**, with

half-maximal activation occurring in the presence of 0.1 mM bovine (b) **PTH**-(1-34). Immunopptn. of exts. of 32P-labeled cells using a monoclonal **antibody** to the **PTH**/PTHrP receptor revealed the presence of a major 32P-labeled protein of approx. 85 kDa that was not evident in untransfected 293 cells. The bPTH-(1-34) treatment produced a rapid dose-dependent increase in phosphorylation of the 85-kDa receptor, with a maximal effect that was 3.5-fold over basal. Half-maximal phosphorylation occurred with 10 nM bPTH-(1-34), similar to the hormone concn. required for 50% receptor occupancy. Activation of protein kinase A or protein kinase C with forskolin or phorbol 12-myristate 13-acetate also increased **PTH**/PTHrP receptor phosphorylation, but to a lesser degree than **PTH**. Neither of these kinases mediated the effect of **PTH**, as blockade of the protein kinase A pathway (with H-89) or the protein kinase C pathway (with the bisindolylmaleimide GF 109203X) did not **inhibit** bPTH-(1-34)-induced **PTH**/PTHrP receptor phosphorylation. These results suggest that agonist-stimulated **PTH**/PTHrP receptor phosphorylation may involve a non-second messenger-activated kinase, such as a member of the G protein-coupled receptor kinase family.

L9 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:785947 HCAPLUS
DOCUMENT NUMBER: 123:189020
TITLE: Adenyl cyclase and interleukin 6 are downstream effectors of parathyroid hormone resulting in stimulation of bone resorption
AUTHOR(S): Grednfield, Edward M.; Shaw, Steven M.; Gornik, Sandra A.; Banks, Michael A.
CORPORATE SOURCE: Dep. Orthopaedics, Case Western Reserve Univ., Cleveland, OH, 44106-5000, USA
SOURCE: Journal of Clinical Investigation (1995), 96(3), 1238-44
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Parathyroid hormone** and other bone resorptive agents function, at least in part, by inducing osteoblasts to secrete cytokines that stimulate both differentiation and resorptive activity of osteoclasts. The authors previously identified two potentially important cytokines by demonstrating that **parathyroid hormone** induces expression by osteoblasts of IL-6 and leukemia **inhibitory** factor without affecting levels of 14 other cytokines. Although **parathyroid hormone** activates multiple signal transduction pathways, induction of IL-6 and leukemia **inhibitory** factor is dependent on activation of adenyl **cyclase**. This study demonstrates that adenyl **cyclase** is also required for stimulation of osteoclast activity in cultures contg. osteoclasts from rat long bones and UMR106-01 rat osteoblast-like osteosarcoma cells. Since the stimulation by **parathyroid hormone** of both cytokine prodn. and bone resorption depends on the same signal transduction pathway, the authors hypothesized that IL-6 might be a downstream effector of **parathyroid hormone**. The authors found that addn. of exogenous IL-6 mimics the ability of

parathyroid hormone to stimulate bone resorption. More importantly, an **antibody** directed against the IL-6 receptor blocks moderate stimulation of osteoclast activity induced by the hormone. Interestingly, strong stimulation of resorption overcomes this dependence on IL-6. Thus, **parathyroid hormone** likely induces multiple, redundant cytokines that can overcome the IL-6 requirement assocd. with moderate stimulation.

L9 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:183941 HCAPLUS
DOCUMENT NUMBER: 118:183941
TITLE: Gs mediates hormonal inhibition of the calcium pump in liver plasma membranes
AUTHOR(S): Jouneaux, Catherine; Audigier, Yves; Goldsmith, Paul; Pecker, Francoise; Lotersztajn, Sophie
CORPORATE SOURCE: Inst. Natl. Sante, Hop. Henri Mondor, Creteil, 94010, Fr.
SOURCE: Journal of Biological Chemistry (1993), 268(4), 2368-72
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been reported that the calcium pump in liver plasma membranes is coupled to Gs or a Gs-like protein. However, it is shown here that isoproterenol, which activated adenylyl **cyclase** via Gs, had no effect on the calcium pump, while human calcitonin, human **parathyroid hormone**, and mini-glucagon, which **inhibited** this system, did not affect adenylyl **cyclase** activity. In order to det. the nature of the G protein coupled to the calcium pump, the RM **antibody**, raised against the carboxyl-terminal decapeptide of Gs.alpha., which antagonized adenylyl **cyclase** activation by isoproterenol or glucagon, was used. The RM **antibody** specifically blocked calcium pump **inhibition** by mini-glucagon, calcitonin, or **parathyroid hormone**, while it did not affect guanosine 5'-O-(thiotriphosphate) **inhibition**. Its effect was mimicked by the corresponding decapeptide RMHLRQYELL. The AS/7 **antibody**, reactive with Gt.alpha., Gi1.alpha. and Gi2.alpha., was ineffective. Complementation of liver plasma membranes with in vitro translated Gs.alpha.2, the large form of Gs.alpha., led to a 40% decrease in calcium pump activity, with a parallel 2-fold increase in adenylyl **cyclase** activity. In vitro translated Gi1.alpha. did not affect the calcium pump activity, while it evoked a 40% **inhibition** of adenylyl **cyclase** activity. Apparently, the same Gs.alpha. may be coupled either to the calcium pump or to adenylyl **cyclase**. However, Gs is functionally specialized, since it does not ensure cross-talk between the two receptor-effector systems. These results point out the possible compartmentalization of Gs.

L9 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:420887 HCAPLUS
DOCUMENT NUMBER: 117:20887
TITLE: PTH stimulates the proliferation of TE-85 human osteosarcoma cells by a mechanism not involving either increased cAMP or increased secretion of IGF-I, IGF-II or TGF.beta.
AUTHOR(S): Finkelman, Richard D.; Mohan, Subburaman;

Linkhart, Thomas A.; Abraham, Susan M.; Boussy, James P.; Baylink, David J.
CORPORATE SOURCE: Dep. Periodontics, Loma Linda Univ., Loma Linda, CA, USA
SOURCE: Bone and Mineral (1992), 16(2), 89-100
CODEN: BOMIET; ISSN: 0169-6009
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of **parathyroid hormone** (**PTH**) on a human bone cell line using TE-85 human osteosarcoma cells as a model were investigated. After 24 h treatment, **PTH** caused an increase in cell proliferation as measured by cell counts and [3H]thymidine incorporation. Proliferation was not **inhibited** by an antitransforming growth factor .beta. (TGF.beta.) **antibody** which could abolish stimulation by exogenous TGF.beta.. **PTH** did not stimulate cAMP prodn., alk. phosphatase activity, or prodn. of insulin-like growth factors I or II (IGF-I or IGF-II) in TE-85 cells. Although basal TE-85 proliferation was slowed by incubation with the Ca channel blocking agent verapamil, **PTH** still caused an increase in growth rate. Thus, **PTH** directly stimulates TE-85 proliferation via a mechanism not involving increased adenylate **cyclase** activity or increased secretion of IGF-I, IGF-II, or TGF.beta. and may stimulate bone formation in vivo by activating some other mitogenic signal to increase bone cell proliferation.

L9 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:507044 HCAPLUS
DOCUMENT NUMBER: 115:107044
TITLE: Altered differentiation of limb bud cells by transforming growth factors-.beta. isolated from bone matrix and from platelets
AUTHOR(S): Schoenfeld, Hans Joachim; Poeschl, Bernd; Wessner, Bruno; Kistler, Andreas
CORPORATE SOURCE: Cent. Res. Units, F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.
SOURCE: Bone and Mineral (1991), 13(3), 171-89
CODEN: BOMIET; ISSN: 0169-6009
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A crude ext. of demineralized bone matrix caused an altered differentiation of limb bud cells which was seen within 5 days in culture. Using this bioassay system 2 factors were purified to homogeneity and were found, according to their N-terminal sequences, to correspond to transforming growth factor-B1 (TGF-.beta.1) and TGF-.beta.2 isolated from platelets. Biochem. analyses and biol. studies (mol. mass detn., **inactivation** by reducing agents and proteases, **antibody** neutralization, competitive binding to TGF-.beta. receptors, and influence on protein expression) provided addnl. evidence that the 2 proteins isolated from demineralized bone matrix were apparently identical to TGF-.beta.1 and TGF-.beta.2. Proteoglycan content, alk. phosphatase activity, and response of the cells to **parathyroid hormone**-stimulated adenylate **cyclase** were quant. changed by the factors. Culturing limb bud cells on polycarbonate membranes resulted in a rapid and extensive growth and differentiation of the cells to palpable tissue pieces. Relative to controls distinct cell and tissue morphol. was obsd. macroscopically

and in histol. sections of these tissue pieces.

L9 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:221798 HCAPLUS
DOCUMENT NUMBER: 114:221798
TITLE: Osteolytic activity of Walker carcinosarcoma 256 is due to parathyroid hormone-related protein (PTHrP)
AUTHOR(S): Scharla, S. H.; Minne, H. W.; lempert, Uta G.; Krieg, P.; Rappel, Sigrid; Maurer, Elke; Grohe, Ursula; Ziegler, R.
CORPORATE SOURCE: Abt. Inn. Med. I, Endokrinol. Stoffwechsel, Univ. Heidelberg, Heidelberg, D-6900, Germany
SOURCE: Hormone and Metabolic Research (1991), 23(2), 66-9
CODEN: HMMRA2; ISSN: 0018-5043
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The hypercalcemic Walker carcinosarcoma 256 of the rat is an animal model for humoral hypercalcemia of malignancy, and previous in vivo studies suggested the prodn. of a **parathyroid hormone**-related protein)PTHrP) by the Walker tumor. Therefore, immunoreactive PTHrP in serum-free conditioned medium from cells derived from this tumor was measured using an **antibody** raised against human PTHrP(1-34). Walker tumor cell conditioned medium (WCM) displaced 125I-labeled hPTHrP(1-34) from the **antibody** in a dose-dependent manner, whereas control medium contained no immunoreactive rat **parathyroid hormone** (rat **PTH**) by the Walker tumor cells was detected using a midregional RIA for rat **PTH**. WCM stimulated adenylate **cyclase** in osteoblast-like cells, the dose-response curve paralleling that of hPTHrP(1-34). This effect could be **inhibited** by the **PTH** antagonist (Nle8,Nle18,Tyr34)bPTH(3-34) and by the addn. of anti-hPTHrP(1-34) **antibody**. Bone resorbing activity of WCM in organ culture (calvaria of fetal rats) was not **inhibited** by indomethacin and glucocorticoids, suggesting a prostaglandin-independent mechanism of osteoclast activation in this model.

L9 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:545709 HCAPLUS
DOCUMENT NUMBER: 113:145709
TITLE: Release of parathyroid hormonelike peptides by fetal rat long bones in culture
AUTHOR(S): Bergmann, P.; Nijs-De Wolf, N.; Pepersack, T.; Corvilain, J.
CORPORATE SOURCE: Dep. Clin. Chem., Hop. Univ. Brugmann, Brussels, 1020, Belg.
SOURCE: Journal of Bone and Mineral Research (1990), 5(7), 741-53
CODEN: JBMREJ; ISSN: 0884-0431
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Culture medium conditioned with fetal rat long bones stimulated cAMP prodn. by renal cortical membranes. This **cyclase** -stimulating activity (CSA) was retained by an ultrafiltration membrane with a mol. wt. cutoff of 5000; 3 biol. active peaks with approx. mol. wts. of 18,000-25,000, 9000-12,000, and 4000-6000 were

sepd. by HPLC. The biol. activity was destroyed by trypsin digestion. The stimulation of adenylate **cyclase** by the medium and by the 3 peaks was **inhibited** by [N-Leu8,18,Tyr34]**parathyroid hormone** -(3-34)-amide and by [Tyr34]**parathyroid hormone** -(7-34)amide. Preincubation of the bone culture medium and of the 3 peaks with an **antibody** raised against human **parathyroid hormone**-(1-34) did not decrease the biol. activity more than incubation with nonimmune serum. However, the biol. activity of the 3 active peaks was suppressed after preincubation with an antiserum directed against the N-terminal region of the **parathyroid hormone**-related peptide of malignancy. The release of CSA into the bone culture medium was enhanced by **parathyroid hormone** induction and by 1,25-dihydroxycholecalciferol. It was decreased by calcitonin. Thus, fetal murine bones in culture release peptides that stimulate the adenylate **cyclase** of renal cortical membranes. These peptides are antigenically similar to the **parathyroid hormone** related peptide of malignancy. Their release from bones is modulated by hormones that control bone resorption.

L9 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:16613 HCAPLUS
DOCUMENT NUMBER: 112:16613
TITLE: Modulation of responsiveness of the adenylate cyclase system in avian chondroprogenitor cells by pertussis toxin, PTH, and PGE2
AUTHOR(S): Pines, Mark; Yosif, Bernard; Hurwitz, Shmuel
CORPORATE SOURCE: Inst. Anim. Sci., Agric. Res. Organ., Bet Dagan, 50250, Israel
SOURCE: Journal of Bone and Mineral Research (1989), 4(5), 743-50
CODEN: JBMREJ; ISSN: 0884-0431
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chondroprogenitor cells, derived from avian tibia epiphyseal growth plate, were cultured in vitro. Incubation of these cells with pertussis toxin augmented their cAMP response to **parathyroid hormone** (**PTH**), attenuated the response to forskolin, but did not modify the response to PGE2. Pertussis toxin modulation of the cAMP response was accompanied by ADP ribosylation of 2 proteins with mol. wts. of 39 and 40 kilodaltons (kD). Using specific **antibodies**, the 39-kD protein was identified as the **inhibitory** guanine nucleotide binding protein (Gi) of the adenylate **cyclase** system. The other ADP-ribosylated protein has not been identified. Preincubation of the chondroprogenitor cells with **PTH** or PGE2 resulted in time-dependent heterologous desensitization of the cAMP response to a 2nd challenge of either hormone. The cells did not recover from the desensitization for .gtoreq.18 h after removal of the hormones. **PTH** and PGE2 treatment did not affect the cAMP response to forskolin and cholera toxin. The **PTH**-dependent cAMP prodn. was also not altered by forskolin treatment. **PTH** homologous desensitization was not affected by pertussis toxin treatment, but the heterologous desensitization due to PGE2 was significantly attenuated. Evidently, exposure of chondroprogenitor cells to **PTH** and PGE2 results in heterologous

desensitization of the cAMP response. The desensitization is not due to changes in the adenylate **cyclase** activity. The pertussis toxin-sensitive G proteins are involved in the **PTH** heterologous rather than homologous desensitization of the cAMP response.

L9 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:625618 HCAPLUS
DOCUMENT NUMBER: 111:225618
TITLE: Opposing effects of fibroblast growth factor and pertussis toxin on alkaline phosphatase, osteopontin, osteocalcin, and type I collagen mRNA levels in ROS 17/2.8 cells
AUTHOR(S): Rodan, Sevgi B.; Wesolowski, Gregg; Yoon, Kyonggeun; Rodan, Gideon A.
CORPORATE SOURCE: Dep. Bone Biol. Osteoporosis Res., Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: Journal of Biological Chemistry (1989), 264(33), 19934-41
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In rat osteosarcoma (ROS 17/2.8) cells, which express osteoblastic features in culture, basic fibroblast growth factor (bFGF) reduces the level of alk. phosphatase, type I collagen, and osteocalcin mRNA and increases osteopontin mRNA, independent of growth stimulation. The fibroblast growth factor (FGF) effects are dose-dependent (EC50 about 6 pM) and are detected 24 h after addn. of the growth factor. The bFGF also reduces **parathyroid hormone** -stimulatable adenylate **cyclase** and alk. phosphatase activity in these cells. Concomitant treatment with pertussis toxin (20 ng/mL) opposes the FGF effects. Although cAMP elevating agents mimic pertussis toxin action on some parameters, they produce opposite effects on others, indicating that antagonism between pertussis toxin and bFGF is not mediated by cAMP. The bFGF caused a small redn. in steady state NAD-dependent ADP-ribosylation and had no detectable effects on the steady-state levels of the Gi.alpha. (.alpha. subunit of the **inhibitory** G protein) 1, 2, and 3, visualized with specific **antibodies** in these cells. Although the site of interaction of pertussis toxin and FGF remains to be detd., there findings suggest sep. control of growth and differentiation by bFGF and show that pertussis toxin treatment can modulate differentiation in these cells, presumably via Gi proteins.

L9 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:490705 HCAPLUS
DOCUMENT NUMBER: 111:90705
TITLE: Estradiol effects on proliferation, messenger ribonucleic acid for collagen and insulin-like growth factor-I, and parathyroid hormone-stimulated adenylate cyclase activity in osteoblastic cells from calvariae and long bones
AUTHOR(S): Ernst, Matthias; Heath, Joan K.; Rodan, Gideon A.
CORPORATE SOURCE: Dep. Bone Biol. Osteoporosis Res., Merck, Sharp, and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: Endocrinology (1989), 125(2), 825-33
CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The estrogen responsiveness of osteoblastic cells was examd. by using the exptl. immortalized calvarial cell lines RCT-1 and RCT-3 as well as primary cultures of calvarial and trabecular bone cells. Estradiol (E2) treatment reduced **parathyroid hormone** (**PTH**)-stimulated adenylate **cyclase** activity by 20-30% in RCT cells; the max. effect was obsd. after treatment with 1 nM E2 for .gtoreq.4 h. In trabecular cells, E2 decreased **PTH**-stimulated adenylate **cyclase** activity by 60-80%. After a lag period of .gtoreq.48 h, E2 treatment (0.01-10 nM) increased cell no. and [3H]thymidine incorporation in both RCT-3 cells and primary cultures of trabecular cells to 20-60% above control values. Half-maximal effects were obsd. at .apprx.1 nM E2. **Antibodies** against insulin-like growth factor-I (IGF-I) **inhibited** the E2-induced proliferation in a dose-dependent manner without affecting basal growth. Furthermore, E2 treatment increased the steady state levels of IGF-I mRNA 2-2.5-fold in calvarial and RCT-3 cells compared to control levels. In addn., E2 (10 nM) increased the level of collagen mRNA >2-fold and opposed the suppression of collagen mRNA produced by **PTH** treatment. The E2 effects were specific to 17.beta.-E2, since they were not obsd. with the biol. less active stereoisomer 17.alpha.-E2 and were blocked by the E2 antagonist tamoxifen (1 .mu.M). Thus, for osteoblastic cells in culture, E2 can directly stimulate proliferation as well as collagen and IGF-I mRNA while decreasing **PTH** responsiveness; these effects could explain the anabolic and anticatabolic effects of E2 on bone.
IT **9002-64-6, Parathyroid hormone**
RL: BIOL (Biological study)
(adenylate **cyclase** stimulation by, in osteoblast, estradiol **inhibition** of)

L9 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:886 HCAPLUS
DOCUMENT NUMBER: 106:886
TITLE: Demonstration of anti-receptor autoantibodies induced by treatment with synthetic hPTH 1-34
AUTHOR(S): Ermias, A.; Defontaine, A.; Audran, M.; Tanguy, G.; Bidet, M.; Jallet, P.
CORPORATE SOURCE: CHU, Angers, Fr.
SOURCE: Journal de Biophysique et de Biomecanique (1986), 10(2, Suppl.), 139-41
CODEN: JBBIE5; ISSN: 0766-5717
DOCUMENT TYPE: Journal
LANGUAGE: French
AB Treatment of an osteoporotic woman with human **parathyroid hormone** (1-34) [hPTH (1-34)] [52232-67-4] resulted in clin. signs of hypoparathyroidism assocd. with elevated plasma **PTH** [**9002-64-6**] levels and the appearance of an anti-**PTH antibody** in the serum. IgG from the patient serum displaced 125I-hPTH (1-34) receptor binding and **inhibited** adenylate **cyclase** in chicken kidney membrane prepns. Evidently, the injection of hPTH (1-34) produced an immunol. cascade consisting of the appearance of anti-**PTH antibodies** followed by anti-iodiotypic **PTH antibodies** which due to their structural analogy behaved like **PTH** anti-receptor **antibodies**.

L9 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:603837 HCAPLUS
DOCUMENT NUMBER: 105:203837
TITLE: Effect of sixth component of complement of the prostaglandin E1 stimulated adenyl cyclase activity in rat calvaria
AUTHOR(S): Watanabe, Norio; Abiko, Yoshimitsu
CORPORATE SOURCE: Sch. Dent., Nihon Univ., Matsudo, Japan
SOURCE: General Pharmacology (1986), 17(5), 525-9
CODEN: GEPHDP; ISSN: 0306-3623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human serum enhanced the PGE1 [745-65-3]-stimulated adenyl **cyclase** [**9012-42-4**] activity in membrane-rich fraction of rat calvaria, but heated serum did not. Human complement C6 (C6) [80295-56-3] enhanced the PGE1-stimulated adenyl **cyclase** activity. C6 did not enhance the **parathormone** [**9002-64-6**]-stimulated adenyl **cyclase** activity. The enhancement of the PGE1-stimulated adenyl **cyclase** activity with C6 was due to increasing Vmax. The enhancement of the enzyme activity with C6 was **inhibited** with anti-C6 **antibody**. Adenyl **cyclase** was not activated with C6 alone.

L9 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:603607 HCAPLUS
DOCUMENT NUMBER: 105:203607
TITLE: Cyclic AMP-dependent and -independent effects on tissue-type plasminogen activator activity in osteogenic sarcoma cells; evidence from phosphodiesterase inhibition and parathyroid hormone antagonists
AUTHOR(S): Allan, Elizabeth H.; Hamilton, John A.; Medcalf, Robert L.; Kubota, Minoru; Martin, T. John
CORPORATE SOURCE: Repatriation Gen. Hosp., Univ. Melbourne, Heidelberg, 3081, Fed. Rep. Ger.
SOURCE: Biochimica et Biophysica Acta (1986), 888(2), 199-207
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The plasminogen [9001-91-6] activator (PA) in clonal osteogenic sarcoma cells of rat origin (UMR 106-01 and UMR 106-06) and in osteoblast-rich rat calvarial cells was characterized by using specific **antibodies** to tissue-type PA (tPA). A mol. wt. (Mr) value of 75,000 by SDS-PAGE and fibrin autoradiog. supports this characterization. There was also evidence for an Mr 105,000 component, which could be due to a proteinase-**inhibitor** complex. The mechanism of regulation of this tPA activity was studied in the clonal osteogenic sarcoma cells. **Parathyroid hormone** (**PTH**) [**9002-64-6**] and PGE2 [363-24-6], which increase cAMP [60-92-4] prodn. in the sarcoma cells, also increased tPA activity. The sensitivity and magnitude of the tPA response to **PTH** and PGE2 were increased by simultaneous treatment with IBMX at drug concns. which had little effect themselves on tPA activity. In UMR 106-06 cells, which unlike UMR 106-01 cells show a cAMP response to calcitonin

[9007-12-9], tPA activity was also increased in response to calcitonin, and the effect was enhanced by IBMX. 1,25-Dihydroxyvitamin D3 [32222-06-3] also increased tPA activity in the cells, but this response was not modified by IBMX. Synthetic peptide antagonists of **PTH**-responsive adenylate **cyclase** [**9012-42-4**], 3-34-[34Tyr]-human **PTH** amide [91314-82-8] and 5-34-[34Tyr]-human **PTH** amide [89072-32-2], **inhibited** the **PTH**-induced increase in tPA activity over the same concn. range at which they **inhibited** cAMP prodn., but the antagonist peptides had no effect on the tPA responses to PGE2, calcitonin, or 1,25-dihydroxyvitamin D3. Thus, cAMP mediates the actions of **PTH**, PGE2, and calcitonin in increasing tPA activity in the clonal osteogenic sarcoma cells. 1,25-Dihydroxyvitamin D3, on the other hand, increases tPA activity through a mechanism independent of cAMP.

L9 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:590337 HCAPLUS
DOCUMENT NUMBER: 103:190337
TITLE: Identification of a monoclonal **antibody** which interacts with the parathyroid hormone receptor-adenylate cyclase system in murine bone
AUTHOR(S): Weinshank, Richard L.; Cain, Christopher D.; Vasquez, Nora P.; Luben, Richard A.
CORPORATE SOURCE: Dep. Biochem., Univ. California, Riverside, CA, 92521, USA
SOURCE: Molecular and Cellular Endocrinology (1985), 41(2-3), 237-46
CODEN: MCEND6; ISSN: 0303-7207
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monoclonal **antibodies** which bind specifically to mouse bone cells were produced and then selected for their ability to **inhibit parathyroid hormone** (**PTH**) responses in mouse cranial bone treated with the (1-34) bovine **PTH** [bPTH(1-34)] [12583-68-5]. One clone, designated 3-6, characterized as an IgM(.kappa.), significantly **inhibited** the accumulation of cAMP [60-92-4] in response to bPTH(1-34) at concns. of 10-9-10-7M. This **antibody** was subsequently isolated by gel filtration and shown to bind to intact mouse calvariae, with satn. binding occurring at 3 .mu.g IgM/mL. A maximal **inhibition** of .apprx.70% of the cAMP accumulation produced in response to 2.5 .times. 10-8M (100 ng/mL) bPTH(1-34) was obtained with 7 .mu.g of the purified 3-6 IgM/mL. At this concn. of 3-6 IgM, the half-maximal dose of **PTH** for activation of cAMP accumulation was increased from 5 .times. 10-9M to 2 .times. 10-8M with no redn. in maximal levels of cAMP prodn. The utility of this **antibody** as an **inhibitor** was further tested by its ability to block the binding of an iodinated **PTH** analog 125I-labeled [Nle8,Nle18,Tyr34]-bPTH(1-34) [59029-34-4] to mouse cranial bone. The 3-6 IgM at a concn. of 5 .times. 10-8M **inhibited** 70% of the specific binding of the 125I-labeled analog. In the absence of **parathyroid hormone**, 2 .times. 10-8M 3-6 IgM produced a 4-fold increase in cAMP above basal levels, as compared to 40-fold maximal increases obsd. with **PTH**, indicating a partial **PTH** agonist activity of this **antibody**. When tested for effects on other hormones,

3-6 IgM did not **inhibit** cAMP accumulation produced in response to salmon calcitonin, epinephrine, PGE2, or cholera toxin. Apparently the 3-6 monoclonal IgM is specific for the **PTH** receptor or a component of the **PTH** receptor-adenylate **cyclase** [**9012-42-4**] system and this or similar **antibodies** will serve as useful reagents for future mol. characterization of this receptor.

L9 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1979:201781 HCAPLUS
DOCUMENT NUMBER: 90:201781
TITLE: Autoantibodies to parathyroid hormone receptor
AUTHOR(S): Jueppner, H.; Bialasiewicz, A. A.; Hesch, R. D.
CORPORATE SOURCE: Dep. Endocrinol., Med. Hochsch., Hannover, Fed. Rep. Ger.
SOURCE: Lancet (1978), 2(8102), 1222-4
CODEN: LANCAO; ISSN: 0023-7507
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Autoantibodies which block the binding of **parathyroid hormone** (I) to membrane receptors for I were detected in the serums of 49 out of 50 uremic patients with secondary hyperparathyroidism. The **antibodies** were species-specific and their presence in the serum was unaffected by dialysis. **Inhibition** of binding appeared to be related to the rise in C-regional I levels and the duration of uremia. The prodn. of cyclic AMP by I-stimulated adenyl **cyclase** was reduced by the blocking **antibodies**. Thus secondary hyperparathyroidism in uremia is a receptor-**antibody** disease; the **antibodies** may act by modifying the affinity of the receptors for I or by reducing the concn. of receptors available.

L9 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:573998 HCAPLUS
DOCUMENT NUMBER: 89:173998
TITLE: Evidence for glomerular receptors for parathyroid hormone
AUTHOR(S): Sraer, J.; Sraer, J. D.; Chansel, D.; Jueppner, H.; Hesch, R. D.; Ardaillou, R.
CORPORATE SOURCE: Inst. Natl. Sante Rech. Med., Tenon Hosp., Paris, Fr.
SOURCE: American Journal of Physiology (1978), 235(2), F96-F103
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rat renal glomerular receptors for **parathyroid hormone** (**PTH**) [**9002-64-6**] were demonstrated by 2 techniques; direct binding studies of 3H-labeled (1-34)-human **parathyroid hormone** (I) [52232-67-4] and an indirect approach using 125I-labeled specific **antibodies** directed against either I or (1-84)-bovine **PTH**. Binding equil. was reached both at increasing incubation times and increasing **PTH** concns. I-3H binding was **inhibited** by unlabeled hormone and its analogs, but by neither unrelated peptides nor **inactivated PTH**. Addn. of an excess of unlabeled I at equil. produced release of the

tritiated hormone from its receptors. I-3H did not bind to nontarget tissues, but there was a close relation between I-3H binding and adenylate **cyclase** [**9012-42-4**] stimulation by this tracer, with both processes displaying similar KD values close to 10-7 M. The peptides which competed with I-3H for its binding sites were potent stimulators of adenylate **cyclase** activity, whereas those without effect on **PTH** binding were also inactive on this enzyme. Nonspecific binding represented 20-33% of total binding. Binding was pH and temp. dependent, max. binding being obsd. at pH 7.3 and 10.degree.. Binding also increased with Ca concn. in the range 0.01-1 mM. The effect of **PTH** on glomerular filtration rate may involve a direct interaction with **PTH** binding sites in the renal glomeruli.

L9 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:586869 HCAPLUS
DOCUMENT NUMBER: 85:186869
TITLE: **Inhibition** of **PTH** receptor binding and **PTH** mediated adenylate **cyclase** activity by somatostatin
AUTHOR(S): Jueppner, H.; Hesch, R. D.
CORPORATE SOURCE: Dep. Med., Med. Hochsch. Hannover, Hannover, Fed. Rep. Ger.
SOURCE: Biochemical and Biophysical Research Communications (1976), 72(3), 945-51
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **inhibitory** effect of somatostatin on the binding of bovine **parathyroid hormone** (bPTH) [**9002-64-6**] to the receptor of a target organ was studied using the labeled **antibody** method and a partially purified chicken renal membrane prepn. with a high affinity for bPTH. BPTH binding to the receptor was diminished up to 47% in the presence 1-Ala-somatostatin [38916-34-6], whereas 1-Tyr-somatostatin [59481-23-1] was without effect. In contrast, similar effects on biol. activity were found in an adenylate **cyclase** [**9012-42-4**] assay with both peptides. On comparing the amino acid sequences of bPTH and 1-Ala-somatostatin, 2 identical residues could be identified. Somatostatin and bPTH apparently exhibit similar affinity for the ovine receptor because of the identical first amino acid which is essential for initial binding.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:44:42 ON 12 AUG 2003)
L10 82 SEA ABB=ON PLU=ON L9
L11 48 SEA ABB=ON PLU=ON L10 AND (MEAS? OR QUANT? OR DETERM? OR DETECT? OR DET## OR SCREEN? OR MONITOR?)
L12 16 DUP REM L11 (32 DUPLICATES REMOVED)

L12 ANSWER 1 OF 16 MEDLINE on STN
ACCESSION NUMBER: 1999221725 MEDLINE
DOCUMENT NUMBER: 99221725 PubMed ID: 10205244
TITLE: Dopamine-1 receptor coupling defect in renal proximal tubule cells in hypertension.
AUTHOR: Sanada H; Jose P A; Hazen-Martin D; Yu P Y; Xu J; Bruns D E; Phipps J; Carey R M; Felder R A
CORPORATE SOURCE: University of Virginia Health Sciences Center,

Charlottesville, VA, USA.
CONTRACT NUMBER: DK39308 (NIDDK)
DK44756 (NIDDK)
HL23081 (NHLBI)
SOURCE: HYPERTENSION, (1999 Apr) 33 (4) 1036-42.
Journal code: 7906255. ISSN: 0194-911X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990511
Last Updated on STN: 19990511
Entered Medline: 19990429

AB The ability of the dopamine-1 (D1)-like receptor to stimulate adenylyl **cyclase** (AC) and phospholipase C (PLC), **inhibit** sodium transport in the renal proximal tubule (RPT), and produce natriuresis is attenuated in several rat models of hypertension. Since the **inhibitory** effect of D1-like receptors on RPT sodium transport is also reduced in some patients with essential hypertension, we **measured** D1-like receptor coupling to AC and PLC in cultures of human RPT cells from normotensive (NT) and hypertensive (HT) subjects. Basal cAMP concentrations were the same in NT (n=6) and HT (n=4). However, the D1-like receptor agonist fenoldopam increased cAMP production to a greater extent in NT (maximum response=67+/-1%) than in HT (maximum response=17+/-5%), with a potency ratio of 105. Dopamine also increased cAMP production to a greater extent in NT (32+/-3%) than in HT (14+/-3%). The fenoldopam-mediated increase in cAMP production was blocked by SCH23390 (a D1-like receptor antagonist) and by antisense D1 oligonucleotides in both HT and NT, indicating action at the D1 receptor. The stimulatory effects of forskolin and **parathyroid hormone**-related protein of cAMP accumulation were not statistically different in NT and HT, indicating receptor specificity and an intact G-protein/AC pathway. The fenoldopam-stimulated PLC activity was not impaired in HT, and the primary sequence and expression of the D1 receptor were the same in NT and HT. However, D1 receptor serine phosphorylation in the basal state was greater in HT than in NT and was not responsive to fenoldopam stimulation in HT. These studies demonstrate the expression of D1 receptors in human RPT cells in culture. The uncoupling of the D1 receptor in both rats (previously described) and humans (described here) suggests that this mechanism may be involved in the pathogenesis of hypertension; the uncoupling may be due to ligand-independent phosphorylation of the D1 receptor in hypertension.

L12 ANSWER 2 OF 16 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 97242678 MEDLINE
DOCUMENT NUMBER: 97242678 PubMed ID: 9087677
TITLE: Renal dopamine DA1 receptor coupling with G(S) and G(q/11) proteins in spontaneously hypertensive rats.
AUTHOR: Hussain T; Lokhandwala M F
CORPORATE SOURCE: Institute for Cardiovascular Studies, College of Pharmacy, University of Houston, Texas 77204-5511, USA.
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1997 Mar) 272 (3 Pt 2) F339-46.

Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 20000303
Entered Medline: 19970428

AB The dopamine DA1 receptor transduces its signal via adenylyl **cyclase** and phospholipase C in the renal proximal tubule, which has been suggested to be defective at the level of receptor-G protein coupling in spontaneously hypertensive rats (SHR). We prepared basolateral membranes from Wistar-Kyoto (WKY) rats and SHR to **determine** the coupling of DA1 receptor with G proteins, especially G(q/11). Fenoldopam, a DA1-receptor agonist, produced a time- and concentration-dependent stimulation in 35S-labeled guanosine 5'-O-(3-thiotriphosphate) ([35S]GTPgammaS) binding in WKY rats. Fenoldopam-induced (10 microM) stimulation was significantly **inhibited** by a DA1-receptor antagonist, Sch-23390. Specific **antibodies** against COOH terminals of G(S)alpha and G(q/11)alpha produced 50-60% and 40-50% **inhibition**, respectively, in fenoldopam stimulation of [35S]GTPgammaS binding. Western analysis of basolateral membranes with these **antibodies** revealed the presence of G(S)alpha (45 kDa) and G(q/11)alpha (42 kDa). Fenoldopam stimulation of [35S]GTPgammaS binding was significantly attenuated in SHR compared with WKY rats. **Parathyroid hormone** stimulation of [35S]GTPgammaS binding was similar in SHR and WKY rats, whereas stimulation by phenylephrine was significantly reduced in SHR. Densitometric **quantification** of 42-kDa band showed a reduced amount in SHR, whereas the density of 45-kDa band was not significantly different compared with WKY rats. We provide the direct evidence showing the coupling of DA1 receptor with G(q/11)alpha and G(S)alpha and propose that, in addition to a defect in the receptor-G protein coupling, a reduced amount of G(q/11)alpha observed in the hypertensive animals may also contribute to the diminished dopamine-induced **inhibition** of Na+-K+-adenosinetriphosphatase in SHR.

L12 ANSWER 3 OF 16 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 97:262383 SCISEARCH
THE GENUINE ARTICLE: WP850
TITLE: Renal dopamine DA(1) receptor coupling with G(s) and G(q/11) proteins in spontaneously hypertensive rats
AUTHOR: Hussain T; Lokhandwala M F (Reprint)
CORPORATE SOURCE: UNIV HOUSTON, COLL PHARM, INST CARDIOVASC STUDIES, HOUSTON, TX 77204 (Reprint); UNIV HOUSTON, COLL PHARM, INST CARDIOVASC STUDIES, HOUSTON, TX 77204
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLOGY, (MAR 1997) Vol. 41, No. 3, pp. F339-F346.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0363-6127.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English

REFERENCE COUNT: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The dopamine DA(1) receptor transduces its signal via adenylyl **cyclase** and phospholipase C in the renal proximal tubule, which has been suggested to be defective at the level of receptor-G protein coupling in spontaneously hypertensive rats (SHR). We prepared basolateral membranes from Wistar-Kyoto (WKY) rats and SHR to **determine** the coupling of DA(1) receptor with G proteins, especially G(q/11). Fenoldopam, a DA(1)-receptor agonist, produced a time- and concentration-dependent stimulation in S-35-labeled guanosine 5'-O-(3-thiotriphosphate) ([S-35]GTP gamma S) binding in WKY rats. Fenoldopam-induced (10 mu M) stimulation was significantly **inhibited** by a DA(1)-receptor antagonist, Sch-23390. Specific **antibodies** against COOH terminals of G(s) alpha and G(q/11)alpha produced 50-60% and 40-50% **inhibition**, respectively, in fenoldopam stimulation of [S-35]GTP gamma S binding. Western analysis of basolateral membranes with these **antibodies** revealed the presence of G(s) alpha (45 kDa) and G(q/11)alpha (42 kDa). Fenoldopam stimulation of [S-35]GTP gamma S binding was significantly attenuated in SHR compared with WKY rats. **Parathyroid hormone** stimulation of [S-35]GTP gamma S binding was similar in SHR and WKY rats, whereas stimulation by phenylephrine was significantly reduced in SHR. Densitometric **quantification** of 42-kDa band showed a reduced amount in SHR, whereas the density of 45-kDa band was not significantly different compared with WKY rats. We provide the direct evidence showing the coupling of DA(1) receptor with G(q/11)alpha and G(s) alpha and propose that, in addition to a defect in the receptor-G protein coupling, a reduced amount of G(q/11)alpha observed in the hypertensive animals may also contribute to the diminished dopamine-induced **inhibition** of Na+-K+-adenosinetriphosphatase in SHR.

L12 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 97071101 MEDLINE
DOCUMENT NUMBER: 97071101 PubMed ID: 8914026
TITLE: Parathyroid hormone-related protein **detection** and interaction with NO and cyclic AMP in the renovascular system.
AUTHOR: Massfelder T; Stewart A F; Endlich K; Soifer N; Judes C; Helwig J J
CORPORATE SOURCE: Laboratoire de Physiologie Cellulaire Renale, Faculte de Medicine, Universite Louis Pasteur, CJF INSERM 9409, Strasbourg, France.
SOURCE: KIDNEY INTERNATIONAL, (1996 Nov) 50 (5) 1591-603. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970313
Last Updated on STN: 19980206
Entered Medline: 19970304

AB The presence of **parathyroid hormone**-related protein (PTHrP) in human kidney vasculature and the signal transduction pathways stimulated during PTHrP-induced vasodilation of the rabbit kidney were investigated. Immunostaining of human

kidney revealed the abundant presence of PTHrP in media and intima of all microvessels as well as in macula densa. In isolated perfused rabbit kidney preconstricted with noradrenaline, 10(-5) M Rp-cAMPS, a direct **inhibitor** of protein kinase A, produced comparable **inhibition** of 2.5 x 10(-7) M forskolin- and 10(-7) M PTHrP-induced vasorelaxations. Renal vasorelaxation and renal microvessel adenylyl **cyclase** stimulation underwent comparable desensitization following exposure to PTHrP. Nitric oxide (NO)-synthase **inhibition** by L-NAME (10(-4) M), NO scavenging by an imidazolineoxyl N-oxide (10(-4) M) and guanylyl **cyclase inhibition** by methylene blue (10(-4) M) decreased PTHrP-induced vasorelaxation by 27 to 53%, abolished bradykinin-induced vasorelaxation and did not affect forskolin-induced vasorelaxation. The effects of Rp-cAMPS and L-NAME were not additive on PTHrP-induced vasorelaxation. Damaging endothelium by treating the kidney with either anti-factor VIII-related **antibody** and complement, gossypol or detergent, did not affect PTHrP- or forskolin-induced vasorelaxations but reduced bradykinin-induced vasorelaxation by 53 to 92%. Conversely, endothelial damage did not alter the **inhibitory** action of L-NAME on PTHrP-induced vasorelaxation. In conclusion, PTHrP is present throughout the human renovascular tree and juxtaglomerular apparatus. Activation of both adenylyl **cyclase**/protein kinase A and NO-synthase/guanylyl **cyclase** pathways are directly linked to the renodilatory action of PTHrP in a way that does not require an intact endothelium in the isolated rabbit kidney.

L12 ANSWER 5 OF 16 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 96419038 MEDLINE
DOCUMENT NUMBER: 96419038 PubMed ID: 8821823
TITLE: Regulation of the renal Na-HCO3 cotransporter: V. mechanism of the inhibitory effect of parathyroid hormone.
AUTHOR: Ruiz O S; Qiu Y Y; Wang L J; Arruda J A
CORPORATE SOURCE: Section of Nephrology, University of Illinois, Chicago, USA.
SOURCE: KIDNEY INTERNATIONAL, (1996 Feb) 49 (2) 396-402. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961115

AB **PTH** administration decreases proximal HCO3 reabsorption and **inhibits** the brush border Na-H antiporter. We studied the effect of **PTH** on the renal Na-HCO3 cotransporter and examined whether this effect is mediated through the adenylate **cyclase**/cyclic AMP system or through the phospholipase A pathway. We studied the effect of **PTH** [1-34] on the Na-HCO3 cotransporter activity in rabbit renal basolateral membranes incubated with 50 microM ATP by **measuring** the 22Na uptake in the presence of HCO3 and gluconate. Na-HCO3 cotransporter activity (expressed in nmol/mg protein/3 seconds) was taken as the difference in 22Na uptake in the presence of HCO3 and gluconate.

PTH (10(-10) M) completely **inhibited** Na-HCO3 cotransporter activity from 1.23 +/- 0.14 to -0.58 +/- 0.23, P < 0.001. This effect of **PTH** to **inhibit** the Na-HCO3 cotransporter was prevented by the polyclonal **antibody** against G alpha s indicating that **PTH** acts through G alpha s protein. Because G alpha s stimulates adenylate **cyclase**/cyclic AMP system, we examined the effect of **PTH** in the presence and in the absence of the adenylate **cyclase inhibitor**, dideoxyadenosine (DDA). DDA alone (10(-4) M) stimulated the Na-HCO3 cotransporter activity. In the presence of DDA, the net **inhibitory** effect of **PTH** was the same magnitude as that of control, suggesting the existence of other pathways for the effect of **PTH** on the cotransporter. Calmodulin **inhibition** also partially prevented the effect of **PTH**. To **determine** whether the **inhibitory** effect of **PTH** is mediated at least in part, through phospholipase A, we first examined the effect of **PTH** on arachidonic acid release and then **measured** the Na-HCO3 cotransporter activity in presence and in absence of arachidonic acid or eicosatetraynoic acid (ETA), an **inhibitor** of arachidonic acid metabolism. **PTH** significantly increased the release of arachidonic acid by isolated proximal tubule cells and arachidonic acid **inhibited** the Na-HCO3 cotransporter in basolateral membranes. ETA (3 microM) partially prevented the **inhibitory** effect of **PTH**. In cultured proximal tubule cells, **PTH inhibited** the HCO3-dependent 22Na uptake and ethoxyresorufin, an **inhibitor** of cytochrome P-450, blocked the **inhibitory** effect of **PTH** on the cotransporter. These results demonstrate that **PTH inhibits** the renal Na-HCO3 cotransporter through multiple mechanisms, that are mediated through G proteins, G alpha s and GP, and CaM-KII.

L12 ANSWER 6 OF 16 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 95393875 MEDLINE
DOCUMENT NUMBER: 95393875 PubMed ID: 7664644
TITLE: Agonist-stimulated phosphorylation of the G protein-coupled receptor for parathyroid hormone (PTH) and PTH-related protein.
AUTHOR: Blind E; Bambino T; Nissenson R A
CORPORATE SOURCE: Endocrine Unit, Veterans Administration Medical Center, San Francisco, California 94121, USA.
CONTRACT NUMBER: DK-35323 (NIDDK)
SOURCE: ENDOCRINOLOGY, (1995 Oct) 136 (10) 4271-7. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951020
Last Updated on STN: 20000303
Entered Medline: 19951012

AB The objectives of the present study were to **determine** whether the G protein-coupled receptor for **PTH** and **PTH**-related protein (PTHrP) is subject to agonist-specific phosphorylation and to characterize the relevant kinase(s). The

opossum kidney **PTH**/PTHrP receptor stably expressed in human embryonic kidney 293 cells was coupled to adenylyl **cyclase**, with half-maximal activation occurring in the presence of 0.1 nM bovine (b) **PTH**-(1-34). Immunoprecipitation of extracts of 32P-labeled cells using a monoclonal **antibody** to the **PTH**/PTHrP receptor revealed the presence of a major 32P-labeled protein of approximately 85 kilodaltons that was not evident in untransfected 293 cells. bPTH-(1-34) treatment produced a rapid dose-dependent increase in phosphorylation of the 85-kilodalton receptor, with a maximal effect that was 3.5 +/- 0.7-fold (n = 4) over basal. Half-maximal phosphorylation occurred with 10 nM bPTH-(1-34), similar to the hormone concentration required for 50% receptor occupancy. Activation of protein kinase A or protein kinase C with forskolin or phorbol 12-myristate 13-acetate also increased **PTH**/PTHrP receptor phosphorylation, but to a lesser degree than **PTH**. Neither of these kinases mediated the effect of **PTH**, as blockade of the protein kinase A pathway (with H-89) or the protein kinase C pathway (with the bisindolylmaleimide GF 109203X) did not **inhibit** bPTH-(1-34)-induced **PTH**/PTHrP receptor phosphorylation. These results suggest that agonist-stimulated **PTH**/PTHrP receptor phosphorylation may involve a nonsecond messenger-activated kinase, such as a member of the G protein-coupled receptor kinase family.

L12 ANSWER 7 OF 16 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER:	93155038 MEDLINE
DOCUMENT NUMBER:	93155038 PubMed ID: 8428911
TITLE:	Gs mediates hormonal inhibition of the calcium pump in liver plasma membranes.
AUTHOR:	Jouneaux C; Audigier Y; Goldsmith P; Pecker F; Lotersztajn S
CORPORATE SOURCE:	Institut National de la Sante et de la Recherche Medicale Unite 99, Hopital Henri Mondor, Creteil, France.
SOURCE:	JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Feb 5) 268 (4) 2368-72. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199303
ENTRY DATE:	Entered STN: 19930326 Last Updated on STN: 20000303 Entered Medline: 19930308

AB We have reported that the calcium pump in liver plasma membranes is coupled to Gs or a Gs-like protein. However, we show here that isoproterenol, which activated adenylyl **cyclase** via Gs, had no effect on the calcium pump, while human calcitonin, human **parathyroid hormone**, and mini-glucagon, which **inhibited** this system, did not affect adenylyl **cyclase** activity. In order to **determine** the nature of the G protein coupled to the calcium pump, we used the RM **antibody**, raised against the carboxyl-terminal decapeptide of Gs alpha, which antagonized adenylyl **cyclase** activation by isoproterenol or glucagon. The RM **antibody** specifically blocked calcium pump **inhibition** by

mini-glucagon, calcitonin, or **parathyroid hormone**, while it did not affect guanosine 5'-O-(thiotriphosphate) **inhibition**. Its effect was mimicked by the corresponding decapeptide RMHLRQYELL. The AS/7 **antibody**, reactive with Gt alpha, Gi 1 alpha, and Gi2 alpha, was ineffective. Complementation of liver plasma membranes with in vitro translated Gs alpha-2, the large form of Gs alpha, led to a 40% decrease in calcium pump activity, with a parallel 2-fold increase in adenylyl **cyclase** activity. In vitro translated Gi1 alpha did not affect the calcium pump activity, while it evoked a 40% **inhibition** of adenylyl **cyclase** activity. We conclude that a same Gs alpha may be coupled either to the calcium pump or to adenylyl **cyclase**. However, Gs is functionally specialized, since it does not ensure cross-talk between the two receptor-effector systems. These results point out the possible compartmentalization of Gs.

L12 ANSWER 8 OF 16 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 93158197 MEDLINE
DOCUMENT NUMBER: 93158197 PubMed ID: 8430499
TITLE: Studies on chicken polyclonal anti-peptide **antibodies** specific for parathyroid hormone-related protein (1-36).
AUTHOR: Rosol T J; Steinmeyer C L; McCauley L K; Merryman J I; Werkmeister J R; Grone A; Weckmann M T; Swayne D E; Capen C C
CORPORATE SOURCE: Department of Veterinary Pathobiology, Ohio State University, Columbus 43210.
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1993 Jan) 35 (3-4) 321-37.
Journal code: 8002006. ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930326
Last Updated on STN: 19930326
Entered Medline: 19930309

AB Chicken polyclonal **antibodies** were prepared against a synthetic peptide corresponding to the first 36 N-terminal amino acids of **parathyroid hormone**-related protein (PTHrP) by immunizing laying hens. Significant increases of **antibodies** to PTHrP were first **detected** after the second immunization. Production of anti-PTHrP egg yolk **antibodies** peaked 1-2 weeks after the second through sixth immunizations and declined over a period of 2-4 weeks. Polyclonal IgG (IgY) to PTHrP was purified from the egg yolks with high levels of PTHrP specific binding. The anti-PTHrP IgG was used to develop a radioimmunoassay for PTHrP that was able to **detect** 100 pg PTHrP ml-1 (23 pM) in conditioned cell culture medium. The anti-PTHrP IgG was bound to a solid phase and utilized to immunopurify iodinated [Tyr36]-PTHrP (1-36). Anti-PTHrP IgG **inhibited** the in vitro biologic activity of PTHrP as demonstrated by the **inhibition** of adenylate **cyclase** stimulation in a rat osteoblast-like cell line (ROS 17/2.8). The anti PTHrP IgG was immunopurified and utilized for immunohistochemical localization of PTHrP in canine skin. Chickens

were advantageous in producing large amounts of high affinity, neutralizing **antibodies** to a highly conserved mammalian protein such as PTHrP. The **antibodies** will be useful to investigate the function and metabolism of PTHrP in vivo and in vitro.

L12 ANSWER 9 OF 16 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 92309718 MEDLINE
DOCUMENT NUMBER: 92309718 PubMed ID: 1319521
TITLE: In vitro formation and expansion of cysts derived from human renal cortex epithelial cells.
AUTHOR: Neufeld T K; Douglass D; Grant M; Ye M; Silva F; Nadasdy T; Grantham J J
CORPORATE SOURCE: Department of Medicine, University of Kansas Medical Center, Kansas City.
CONTRACT NUMBER: DK38980 (NIDDK)
SOURCE: KIDNEY INTERNATIONAL, (1992 May) 41 (5) 1222-36. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920807
Last Updated on STN: 20000303
Entered Medline: 19920724

AB Acquired renal cysts derive from terminally differentiated tubular epithelium in adults as a consequence of increased epithelial cell proliferation, fluid accumulation and extracellular matrix remodelling. To understand better how human epithelial cysts may be initiated and progressively expand, cells from primary cultures of normal human adult renal cortex were dispersed in polymerized type I collagen. The transparent matrix permitted repeated observation by light microscopy of cyst formation from individual renal cells. The cyst cells reacted strongly with distal nephron histochemical markers (cytokeratin **antibodies** AE1/AE3, epithelial membrane antigen, and Arachis hypogaea lectin) but inconsistently or not at all to markers of proximal tubules (Tetragonolobus purpureas lectin and Phaseolus vulgaris erthroagglutinin lectin). The number of spherical, fluid-filled epithelial cysts that developed in a standardized microscope field **quantified** cyst initiation. Cyst progression was **determined** from the increase in the diameter (surface area) of cysts and represents a hyperplastic event. EGF or TGF alpha, were required in serum-free defined medium to cause cysts to develop from individual epithelial cells dispersed in the matrix; insulin was required as a co-factor. The EC50 for EGF was approximately 0.1 ng/ml, and for insulin 1 microgram/ml. Early cultures of normal cortex formed cysts more efficiently when dispersed in collagen matrix than cells passaged several times before suspension in the gel. Agonists of adenylate **cyclase** (PGE1, AVP, VIP, **PTH**, forskolin, cholera toxin), methylisobutylxanthine, and 8-Br-cAMP, though incapable of causing cyst formation alone in defined medium, enhanced cyst initiation and progression in the presence of EGF and insulin. Angiotensin II, TNF alpha, beta-estradiol, and pertussis toxin had no effect in the absence or presence of EGF and insulin. Pertussis toxin **inhibited** cyst initiation and expansion caused by EGF and forskolin but potentiated cyst initiation and expansion caused by

EGF and PGE1. Cyst formation and expansion were **inhibited** by TGF beta 1 and 2-chloroadenosine. Polarized monolayers of human renal cortical cells grown on permeable membranes were used to independently **quantify** the effects of agonists on the net secretion of solute and water from the basolateral to the apical surface of the cells. PGE1, forskolin, and 8-Br-cAMP stimulated net fluid secretion that was sustained for several days; EGF enhanced forskolin-stimulated fluid secretion. We conclude that the formation and expansion of in vitro cysts derived from solitary human cortex cells depends on the coordinated interplay between cellular proliferation and fluid secretion.(ABSTRACT TRUNCATED AT 400 WORDS)

L12 ANSWER 10 OF 16 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 92248391 MEDLINE
DOCUMENT NUMBER: 92248391 PubMed ID: 1315602
TITLE: PTH stimulates the proliferation of TE-85 human osteosarcoma cells by a mechanism not involving either increased cAMP or increased secretion of IGF-I, IGF-II or TGF beta.
AUTHOR: Finkelman R D; Mohan S; Linkhart T A; Abraham S M; Boussy J P; Baylink D J
CORPORATE SOURCE: Department of Periodontics, Loma Linda University, CA.
CONTRACT NUMBER: AR 31062 (NIAMS)
SOURCE: BONE AND MINERAL, (1992 Feb) 16 (2) 89-100. Journal code: 8610542. ISSN: 0169-6009.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19980206
Entered Medline: 19920605

AB Injections of **parathyroid hormone** (**PTH**) result in increased bone formation in several species. Work in our laboratory and others has shown a stimulation of bone cell proliferation and growth factor production by **PTH**. Our purpose was to study the effects of **PTH** on a human bone cell line using TE-85 human osteosarcoma cells as a model. After 24 h treatment, **PTH** caused an increase in cell proliferation as **measured** by cell counts and [3H]-thymidine incorporation. Proliferation was not **inhibited** by an anti-transforming growth factor beta (TGF beta) **antibody** which could abolish stimulation by exogenous TGF beta. **PTH** did not stimulate cAMP production, alkaline phosphatase activity or production of insulin-like growth factors I or II (IGF-I or IGF-II) in TE-85 cells. Although basal TE-85 proliferation was slowed by incubation with the calcium channel blocking agent verapamil, **PTH** still caused an increase in growth rate. We conclude that **PTH** directly stimulates TE-85 proliferation via a mechanism not involving increased adenylate **cyclase** activity or increased secretion of IGF-I, IGF-II or TGF beta and may stimulate bone formation in vivo by activating some other mitogenic signal to increase bone cell proliferation.

L12 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 91322561 MEDLINE
DOCUMENT NUMBER: 91322561 PubMed ID: 1650618
TITLE: Altered differentiation of limb bud cells by transforming growth factors-beta isolated from bone matrix and from platelets.
AUTHOR: Schonfeld H J; Poschl B; Wessner B; Kistler A
CORPORATE SOURCE: Central Research Unit, F. Hoffmann-La Roche Ltd., Basle, Switzerland.
SOURCE: BONE AND MINERAL, (1991 Jun) 13 (3) 171-89.
Journal code: 8610542. ISSN: 0169-6009.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19910929
Last Updated on STN: 19910929
Entered Medline: 19910912

AB A crude extract of demineralized bone matrix caused an altered differentiation of limb bud cells which was seen within 5 days in culture. Using this bioassay system we purified two factors to homogeneity and found that according to their N-terminal sequences they corresponded to TGF-beta 1 and TGF-beta 2 isolated from platelets. Biochemical analyses and biological studies (molecular mass **determination, inactivation** by reducing agents and proteases, **antibody** neutralization, competitive binding to TGF-beta receptors and influence on protein expression) provided additional evidence that the two proteins isolated from demineralized bone matrix were apparently identical to TGF-beta 1 and TGF-beta 2. Proteoglycan content, alkaline phosphatase activity and response of the cells to **PTH** stimulated adenylate **cyclase** were **quantitatively** changed by the factors. Culturing limb bud cells on polycarbonate membranes resulted in a rapid and extensive growth and differentiation of the cells to palpable tissue pieces. Relative to controls distinct cell and tissue morphology was observed macroscopically and in histological sections of these tissue pieces.

L12 ANSWER 12 OF 16 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 91257767 MEDLINE
DOCUMENT NUMBER: 91257767 PubMed ID: 1646150
TITLE: Osteolytic activity of Walker carcinosarcoma 256 is due to parathyroid hormone-related protein (PTHrP).
AUTHOR: Scharla S H; Minne H W; Lempert U G; Krieg P; Rappel S; Maurer E; Grohe U; Ziegler R
CORPORATE SOURCE: Abteilung Innere Medizin I, Endokrinologie und Stoffwechsel, Klinikum der Universitat Heidelberg, Germany.
SOURCE: HORMONE AND METABOLIC RESEARCH, (1991 Feb) 23 (2) 66-9.
Journal code: 0177722. ISSN: 0018-5043.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910802
Last Updated on STN: 19980206

Entered Medline: 19910716

AB The hypercalcemic Walker carcinosarcoma 256 of the rat is an animal model for humoral hypercalcemia of malignancy. Previous in vivo studies suggested the production of a **parathyroid hormone**-related protein (PTHrP) by the Walker tumor. Therefore, we have **measured** immunoreactive PTHrP in serum-free conditioned medium from cells derived from this tumor using an **antibody** raised against human PTHrP(1-34). Walker tumor cell conditioned medium (WCM) displaced 125I-hPTHrP(1-34) from the **antibody** in a dose dependent manner, whereas control medium contained no immunoreactive PTHrP. In contrast, we **detected** no secretion of immunoreactive rat **parathyroid hormone** (rat **PTH**) by the Walker tumor cells using a midregional radioimmunoassay for rat **PTH**. WCM stimulated adenylate **cyclase** in osteoblast like cells, the dose-response curve paralleling that of hPTHrP(1-34). This effect could be **inhibited** by the **PTH** antagonist (8Nle, 18Nle, 34Tyr)bPTH(3-34) and by the addition of anti-hPTHrP(1-34) **antibody**. Bone resorbing activity of WCM in organ culture (calvaria of fetal rats) was not **inhibited** by indomethacin and glucocorticoids, suggesting a prostaglandin independent mechanism of osteoclast activation in this model.

L12 ANSWER 13 OF 16 MEDLINE on STN
ACCESSION NUMBER: 90115818 MEDLINE
DOCUMENT NUMBER: 90115818 PubMed ID: 2153281
TITLE: Parathyroid hormone-related peptide gene is expressed in the mammalian central nervous system.
AUTHOR: Weir E C; Brines M L; Ikeda K; Burtis W J; Broadus A E; Robbins R J
CORPORATE SOURCE: Section of Comparative Medicine, Yale University School of Medicine, New Haven, CT 06510.
CONTRACT NUMBER: AR30102 (NIAMS)
NS26362 (NINDS)
NSO6208 (NINDS)
+
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Jan) 87 (1) 108-12.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19980206
Entered Medline: 19900209

AB A **parathyroid hormone**-related peptide (PTHRP) has been identified in human tumors associated with the syndrome of humoral hypercalcemia of malignancy. While **parathyroid hormone** (**PTH**) gene expression appears to be limited to the parathyroid glands, PTHRP mRNA has been identified in a variety of normal tissues. To investigate the apparent expression of the PTHRP in the central nervous system, we examined extracts of whole rat brain for PTHRP bioactivity by **measuring** adenylate **cyclase**-stimulating activity (ACSA) in a

PTH-sensitive assay. Extracts consistently contained ACSA and this activity was completely **inhibited** by a PTHRP antiserum but was unaffected by a **PTH** antiserum. ACSA was found in a number of anatomic subregions of rat brain, being greatest in the cortex and telencephalon. RNase protection analysis revealed PTHRP transcripts in total RNA prepared from whole rat brain and from the same anatomic subregions. By in situ hybridization histochemistry, we found that the highest levels of PTHRP gene expression occurred in neurons of the cerebral cortex, hippocampus, and cerebellar cortex. These studies demonstrate that both PTHRP mRNA and biological activity are present in a number of regions of rat brain. The widespread expression of this peptide by multiple types of neurons suggests that the PTHRP may play a general role in neuronal physiology.

L12 ANSWER 14 OF 16 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 90062101 MEDLINE
DOCUMENT NUMBER: 90062101 PubMed ID: 2479640
TITLE: Opposing effects of fibroblast growth factor and pertussis toxin on alkaline phosphatase, osteopontin, osteocalcin, and type I collagen mRNA levels in ROS 17/2.8 cells.
AUTHOR: Rodan S B; Wesolowski G; Yoon K; Rodan G A
CORPORATE SOURCE: Department of Bone Biology and Osteoporosis Research, Merck Sharp & Dohme Research Laboratory, West Point, Pennsylvania 19486.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1989 Nov 25) 264 (33) 19934-41.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 20021218
Entered Medline: 19891228

AB In rat osteosarcoma (ROS 17/2.8) cells, which express osteoblastic features in culture, basic fibroblast growth factor (bFGF) reduces the level of alkaline phosphatase, type I collagen, and osteocalcin mRNA and increases osteopontin mRNA, independent of growth stimulation. The fibroblast growth factor (FGF) effects are dose dependent (EC50 about 6 pM) and are **detected** 24 h after addition of the growth factor. bFGF also reduces **parathyroid hormone**-stimulatable adenylate **cyclase** and alkaline phosphatase activity in these cells. Concomitant treatment with pertussis toxin (20 ng/ml) opposes the FGF effects. Although cyclic AMP elevating agents mimic pertussis toxin action on some parameters, they produce opposite effects on others, indicating that antagonism between pertussis toxin and bFGF is not mediated by cyclic AMP. bFGF caused a small reduction in steady state NAD-dependent ADP-ribosylation and had no **detectable** effects on the steady-state levels of the Gi alpha (alpha subunit of the **inhibitory** G protein) 1, 2, and 3, visualized with specific **antibodies** in these cells. Although the site of interaction of pertussis toxin and FGF remains to be **determined**, the findings presented here suggest separate control of growth and differentiation by bFGF and show that

pertussis toxin treatment can modulate differentiation in these cells, presumably via Gi proteins.

L12 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 12

ACCESSION NUMBER: 1979:180915 BIOSIS
DOCUMENT NUMBER: BA67:60915
TITLE: AUTO **ANTIBODIES** TO PARATHYROID HORMONE RECEPTOR.
AUTHOR(S): JUEPPNER H; BIALASIEWICZ A A; HESCH R D
CORPORATE SOURCE: MED. HOCHSCH., KARL-WIECHERT ALLEE 9, 3000 HANNOVER 61, W. GER.
SOURCE: LANCET, (1978) 2 (8102), 1222-1224.
CODEN: LANCAO. ISSN: 0023-7507.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Autoantibodies which block the binding of **parathyroid hormone** to membrane receptors for the hormone were **detected** in the sera (especially in the Ig[immunoglobulin]G fraction) of 49 of 50 uremic patients with secondary hyperparathyroidism (patients with high levels of C-regional **parathyroid hormone**). These **antibodies** are species-specific. Their presence in the serum is unaffected by dialysis. **Inhibition** of binding is apparently related to the rise in C-regional **parathyroid-hormone** levels and the duration of uremia. The production of cyclic AMP by **parathyroid-hormone**-stimulated adenyl **cyclase** was reduced by the blocking **antibodies.** Secondary hyperparathyroidism in uremia is another example of a receptor-**antibody** disease. It is not known whether the **antibodies** act by modifying the affinity of the receptors for the hormone or by reducing the concentration of receptors available.

L12 ANSWER 16 OF 16 MEDLINE on STN

ACCESSION NUMBER: 79071774 MEDLINE
DOCUMENT NUMBER: 79071774 PubMed ID: 82734
TITLE: Autoantibodies to parathyroid hormone receptor.
AUTHOR: Juppner H; Bialasiewicz A A; Hesch R D
SOURCE: LANCET, (1978 Dec 9) 2 (8102) 1222-4.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197902
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19790221

AB Autoantibodies which block the binding of **parathyroid hormone** to membrane receptors for the hormone were **detected** in the sera (especially in the IgG fraction) of 49 out of 50 uraemic patients with secondary hyperparathyroidism (patients with high levels of C-regional **parathyroid hormone**). These **antibodies** are species-specific. Their presence in the serum in unaffected by dialysis. **Inhibition** of binding appears to be related to the rise in C-regional **parathyroid-hormone** levels and the

duration of uraemia. The production of cyclic adenosine monophosphate by **parathyroid-hormone**-stimulated adenyl **cyclase** was reduced by the blocking **antibodies**. The findings show that secondary hyperparathyrodism in uraemia is another example of a receptor-**antibody** disease, but it is not known whether the **antibodies** act by modifying the affinity of the receptors for the hormone or by reducing the concentration of receptors available.

```
     FILE 'REGISTRY' ENTERED AT 15:47:40 ON 12 AUG 2003
=> e cip/cn 5
E1            1     CIONIN, PRO- (CIONA INTESTINALIS CLONE P3/CIO-21 REDUC
                    ED)/CN
E2            1     CIOTERONEL/CN
E3            1 --> CIP/CN
E4            1     CIP (HORMONE)/CN
E5            1     CIP 1/CN

=> s e3-e4
              1 CIP/CN
              1 "CIP (HORMONE)"/CN
L13           1 (CIP/CN OR "CIP (HORMONE)"/CN)

=> d ide

L13  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   79748-40-6  REGISTRY
CN   .alpha.7-38-Corticotropin (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   7-38-ACTH
CN   CIP
CN   CIP (hormone)
MF   Unspecified
CI   MAN
LC   STN Files:   CA, CAPLUS, CASREACT, DDFU, DRUGU, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
              10 REFERENCES IN FILE CA (1947 TO DATE)
              10 REFERENCES IN FILE CAPLUS (1947 TO DATE)

     (FILE 'HCAPLUS' ENTERED AT 15:48:27 ON 12 AUG 2003)
L13           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  (CIP/CN OR "CIP
                (HORMONE)"/CN)
L14          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 OR CIP(S)CYCLASE
L15           0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND ANTIBOD?

L14  ANSWER 1 OF 13  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:        2003:534273  HCAPLUS
TITLE:                   An Evaluation of 1-84 PTH Measurement in
                         Relation to Bone Alkaline Phosphatase and Bone
                         Gla Protein in Hemodialysis Patients
AUTHOR(S):               Miwa, Naoko; Nitta, Kosaku; Kimata, Naoki;
                         Watanabe, Yoshihiko; Suzuki, Koichi; Kawashima,
                         Akira; Haga, Masahiro; Watanabe, Ryo-ichiro;
                         Aoki, Takanao; Akiba, Takashi; Nihei, Hiroshi
CORPORATE SOURCE:        Kidney Center, Department of Medicine, Tokyo
                         Women's Medical University, Shinjuku-ku, Tokyo,
```

Japan
SOURCE: Nephron (2003), 94(2), c29-c32
CODEN: NPRNAY; ISSN: 0028-2766
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background/Aim: It has been suggested that higher levels of parathyroid hormone (PTH) are required to maintain normal bone turnover in chronic hemodialysis (HD) patients. Serum PTH levels detd. by intact PTH (i-PTH) assay may overestimate the actual activity of circulating PTH in HD patients. The aim of the present study was to assess the clin. usefulness of whole PTH assay on the evaluation of bone turnover in HD patients. Materials and Methods: We performed measurement of parameters on bone turnover in 179 HD patients (116 men, 63 women; mean age 61.0 .+-. 13.1 yr). Serum whole PTH levels were detd. as cyclase-activating PTH (CAP) by an immunoradiometric assay, and compared with those of i-PTH. **Cyclase**-inactivating PTH (**CIP**) was calcd. as (i-PTH-CAP). The correlations between serum whole PTH levels and clin. parameters such as serum levels of Ca, P, bone alk. phosphatase (BAP), bone Gla protein (BGP), total protein (TP), albumin (Alb), urea nitrogen (SUN), and creatinine (Cr) were analyzed using multivariate anal. Results: The mean values of i-PTH and CAP were 124.1 .+-. 97.4 and 86.9 .+-. 71.6 pg/mL, resp., indicating that the serum CAP levels were about 70% of i-PTH levels. The serum CAP levels significantly correlated with that of i-PTH ($r = 0.959$, $p < 0.001$). Moreover, a significant pos. correlation between serum CAP levels and metabolic bone markers such as BAP ($r = 0.400$, $p < 0.01$) and BGP ($r = 0.481$, $p < 0.01$) was obsd. Stepwise multivariate anal. revealed that serum levels of CAP were significantly detd. by serum levels of Ca, P, Alb, and oral dosage of vitamin D (F ratio = 18.81, adjusted r2 = 0.302). Conclusions: These data suggest that the biol. activity of circulating PTH in HD patients is lower than the levels estd. by conventional i-PTH assay.

L14 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:833498 HCAPLUS
DOCUMENT NUMBER: 137:346149
TITLE: Cyclase inhibiting parathyroid hormone antagonists or modulators and osteoporosis
INVENTOR(S): Cantor, Thomas L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002160945	A1	20021031	US 2001-928047	20010810
US 2003087822	A1	20030508	US 2002-215770	20020809

PRIORITY APPLN. INFO.:
US 2000-224446P P 20000810
US 1999-323606 B2 19990602
US 2000-224447P P 20000810
US 2000-636530 A2 20000810
US 2001-928047 A2 20010810

AB The present invention relates to a novel method for treating a patient that has osteoporosis and the patient may be having administered cyclase activating parathyroid hormone (CAP) or analogs. The patient receives an administration of a **cyclase** inhibiting parathyroid hormone peptide (**CIP**) having an amino acid sequence from between [(PTH2-84) and (PTH34-84), preferably (PTH3-84) and (PTH28-84)], or a conservatively substituted variant thereof exhibiting parathyroid hormone (PTH) antagonist activity in a therapeutically effective, but non-toxic amt. that reduces the occurrence of hypercalcemia or osteosarcoma in the patient resulting from the administration of CAP, and yet, through a CAP rebound effect, is effective in itself in the treatment of osteoporosis.

L14 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:657140 HCAPLUS
DOCUMENT NUMBER: 134:10999
TITLE: Mass-correlated pulsed extraction: theoretical analysis and implementation with a linear matrix-assisted laser desorption/ionization time of flight mass spectrometer
AUTHOR(S): Kovtoun, S. V.; Cotter, R. J.
CORPORATE SOURCE: Department of Pharmacology and Molecular Sciences, Middle Atlantic Mass Spectrometry Laboratory, The Johns Hopkins University, Baltimore, MD, USA
SOURCE: Journal of the American Society for Mass Spectrometry (2000), 11(10), 841-853
CODEN: JAMSEF; ISSN: 1044-0305
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pulsed extn. (PE) of ions produced by matrix-assisted laser desorption/ionization in time-of-flight mass spectrometers greatly improves mass resoln. but, unfortunately, this method is mass dependent. Here the authors report an approach to expand the capabilities of the PE method so as to provide uniform focusing conditions over a wide mass range. Along with an extn. pulse, an addnl. pulse is applied to correct the mass dependency of the std. PE method. The authors describe the algorithm for derivation of this correction pulse waveform, where the 1st-order focusing conditions are valid all along the mass region of interest. Exptl. verification of this method for correction of ion velocities demonstrated better mass resoln. than std. PE over a wide mass range.
IT **79748-40-6**, .alpha.7-38-Corticotropin
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(mass-correlated pulsed extn. in theor. anal. and implementation with a linear matrix-assisted laser desorption/ionization time of flight mass spectrometer)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:251625 HCAPLUS
DOCUMENT NUMBER: 122:24130

TITLE: Effects of pituitary adenylate-cyclase activating peptide (PACAP) on the rat adrenal secretory activity: preliminary in-vitro studies
AUTHOR(S): Andreis, Paola G.; Malendowicz, Ludwik K.; Belloni, Anna S.; Nussdorfer, Gastone G.
CORPORATE SOURCE: Dep. Anatomy, Univ. Padua, Padua, I-35121, Italy
SOURCE: Life Sciences (1994), Volume Date 1995, 56(2), 135-42
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PACAP did not affect secretory activity of dispersed rat adrenocortical cells, but it markedly raised aldosterone (ALDO) and corticosterone (B) prodn. by adrenal slices, contg. both medullary and cortical tissues. The secretagogue effects of PACAP were suppressed by PACAP(6-38), a specific competitive antagonist. Isoprenaline (IP) enhanced ALDO, but not B secretion of adrenal slices, and l-alprenolol (AL) completely blocked IP effect. AL and ACTH-inhibiting peptide (CIP) partially reversed ALDO response to a maximal effective concn. of PACAP; AL did not affect B response to a maximal effective concn. of PACAP, while CIP completely annulled it. Quarters of regenerated adrenocortical autotransplants, that are completely deprived of chromaffin cells, though displaying ALDO and B responses to IP and ACTH, were insensitive to PACAP. The hypothesis is advanced that adrenal medulla plays a pivotal role in the mechanism(s) underlying the adrenocortical secretagogue action of PACAP, being mineralocorticoid and glucocorticoid responses probably mediated by the release by chromaffin cells of catecholamine and ACTH or exclusively ACTH, resp.

IT **79748-40-6, CIP**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pituitary adenylate-**cyclase** activating peptide effects on rat adrenal secretory activity)

L14 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:316305 HCAPLUS
DOCUMENT NUMBER: 120:316305
TITLE: Stimulatory effect of vasoactive intestinal peptide (VIP) on the secretory activity of dispersed rat adrenocortical cells. Evidence for the interaction of VIP with ACTH receptors
AUTHOR(S): Mazzocchi, Giuseppina; Malendiwicz, Ludwik K.; Nussdorfer, Gastone G.
CORPORATE SOURCE: Dep. Anat., Univ. Padua, Padua, 35121, Italy
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1994), 48(5-6), 507-10
CODEN: JSBBEZ; ISSN: 0960-0760
DOCUMENT TYPE: Journal
LANGUAGE: English

AB VIP dose-dependently increased basal, but not submaximally ACTH (10-10 M)-stimulated, aldosterone (ALDO) and corticosterone (B) secretion of dispersed rat capsular and inner adrenocortical cells, resp. The maximal stimulatory effect (60-70% rise) was obtained with a VIP concn. of 10-8 M. [4-Cl-D-Phe6,Leu17]-VIP, a VIP-receptor antagonist (VIP-A), and ACTH-inhibiting peptide (CIP), an ACTH receptor antagonist (both 10-6 M), completely annulled VIP

(10-8 M)-evoked rises in basal ALDO and corticosterone secretions. The ACTH (10-10 M)-enhanced (about 5-fold) prodn. of both hormones was completely reversed by CIP (10-6 M) and only partially reduced (about -30%) by VIP-A (10-6 M). The hypothesis is advanced that the weak secretagogue effect of VIP on dispersed rat capsular and inner adrenocortical cells may be due to its pos. interaction with ACTH receptors.

IT **79748-40-6**, CIP
RL: BIOL (Biological study)
(VIP stimulation of adrenal cortex secretion inhibition by, ACTH receptor in relation to)

L14 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:144379 HCAPLUS
DOCUMENT NUMBER: 116:144379
TITLE: Vasoactive intestinal peptide: autocrine growth factor in neuroblastoma
AUTHOR(S): O'Dorisio, M. Sue; Fleshman, Daniel J.; Qualman, Stephen J.; O'Dorisio, Thomas M.
CORPORATE SOURCE: Coll. Med., Ohio State Univ., Columbus, OH, 43205, USA
SOURCE: Regulatory Peptides (1992), 37(3), 213-26
CODEN: REPPDY; ISSN: 0167-0115
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neuroblastoma the most common solid tumor of children <5 yr of age is derived from neural crest precursors; they synthesize both adrenergic and peptidergic neurotransmitters. This study detd. VIP receptor expression in primary neuroblastoma tumors prior to chemotherapy. The VIP receptor was expressed in 12 of 15 neuroblastoma tumors as detd. by direct binding studies (KD = 1.3-12.4 nM) and VIP-mediated stimulation of adenylate cyclase. The VIP stimulation index for adenylate cyclase in the primary tumor was inversely correlated with the VIP content of the tumor, suggesting that VIP regulates its own receptor expression. Similar observations were made in vitro by comparison of 2 human neuroblastoma cell lines, IMR32 and SKNSH. Both cell lines were demonstrated to express specific, high affinity VIP receptors (KD = 4 nM and 2.5 nM for IMR32 and SKNSH, resp.). IMR32 cells contained very low levels of VIP (0.6 pg VIP/106 cells). Exogenous VIP stimulated adenylate cyclase 22-fold over basal activity and VIP inhibited proliferation of IMR32 cells by 49% in 6-day cultures. On the other hand, SKNSH cells synthesized high levels of VIP (6.3 pg/106 cells), metabolized VIP rapidly and demonstrated a low level of **CIP**-mediated stimulation of adenylate **cyclase** ; their proliferation rate was minimally inhibited by exogenous VIP. These observations help validate the hypothesis that VIP serves as an autocrine growth factor in neuroblastoma.

L14 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:156525 HCAPLUS
DOCUMENT NUMBER: 114:156525
TITLE: Uptake and metabolism of iproplatin in murine L1210 cells
AUTHOR(S): Pendyala, L.; Walsh, J. R.; Huq, M. M.; Arakali, A. V.; Cowens, J. W.; Creaven, P. J.
CORPORATE SOURCE: Dep. Clin. Pharmacol. Ther., Roswell Park Mem. Inst., Buffalo, NY, 14263, USA

SOURCE: Cancer Chemotherapy and Pharmacology (1989), 25(1), 15-18
CODEN: CCPHDZ; ISSN: 0344-5704
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Iproplatin is structurally unique among the platinum (Pt) agents in the clinic because it is a quadrivalent complex. On the basis of the redox parameters for the Pt(IV) and Pt(II) oxidn. states in a chloride system, it has been suggested that Pt(IV) complexes will be reduced to Pt(II) complexes in a biol. environment. To test this hypothesis, uptake and metab. studies of [14C]-iproplatin were carried out in L1210 cells. The L1210 cells raised in DBA2/J mice were incubated in vitro with 50 and 100 .mu.M [14C]-iproplatin at 37 .degree.C in Hanks' balanced salt soln., and total uptake and radioactivity assocd. with acid-insol. fractions were measured for up to 3 h. Under these conditions, the uptake of iproplatin was linear with time and increased with increasing concns. of iproplatin in the medium. At all times measured, >35% of radioactivity was assocd. with the acid-insol. fraction, suggesting binding to macromols. The [14C]-labeled compds. in neutralized acid exts. of cells were sepd. by reverse-phase HPLC. Three labeled compds. were detected; based on chromatog. elution times, they appeared to be iproplatin, cis-dichloro-bis-isopropylamine platinum(II) (CIP), the redn. product of iproplatin, and a third compd. more polar than iproplatin and CIP. The finding of free CIP and the macromol. binding of radioactivity in the cells suggests that iproplatin is reduced intracellularly.

IT **79748-40-6**, CIP
RL: FORM (Formation, nonpreparative)
(formation of, as iproplatin metabolite, in tumor cells)

L14 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:156524 HCAPLUS
DOCUMENT NUMBER: 114:156524
TITLE: Studies on the human metabolism of iproplatin
AUTHOR(S): Pendyala, L.; Krishnan, B. S.; Walsh, J. R.; Arakali, A. V.; Cowens, J. W.; Creaven, P. J.
CORPORATE SOURCE: Dep. Clin. Pharmacol. Ther., Roswell Park Mem. Inst., Buffalo, NY, 14263, USA
SOURCE: Cancer Chemotherapy and Pharmacology (1989), 25(1), 10-14
CODEN: CCPHDZ; ISSN: 0344-5704
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have previously shown that a significant portion of the total platinum in the plasma of patients receiving iproplatin is protein-bound. The authors have also identified cis-dichloro-bis-isopropylamine platinum(II) (CIP) as a major metabolite of iproplatin. To understand the nature of the bound platinum, in vitro comparative protein-binding for iproplatin and CIP was studied. These studies indicate that when CIP is incubated in plasma, protein binding occurs, with a 2.7-h half-life for the disappearance of CIP; the parent complex does not bind and is stable in plasma for at least 48 h. The time dependence of protein binding with CIP suggests the formation of other chem. species from CIP that may be responsible for the obsd. protein binding. The results indicate that in patients receiving the drug, the redn. of iproplatin to CIP must take place intracellularly and that CIP or

its protein-binding derivs. must efflux from the cells into the plasma. Efflux studies carried out to explore this possibility with cells in the whole blood showed that iproplatin was taken up into cells, but the efflux of protein-binding iproplatin metabolites did not occur. To understand further the nature of the metabolites of iproplatin, the authors carried out 195Pt-NMR (NMR) studies with urine from two patients who received a high dose of iproplatin (500 mg/m2). The predominant signals from the 195Pt-NMR corresponded to the divalent platinum complexes and not to tetravalent complexes, indicating that the iproplatin metabolites in urine are divalent in nature.

IT **79748-40-6**, CIP
RL: BIOL (Biological study)
(as iproplatin metabolite, protein binding and urinary excretion of, in humans)

L14 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:97555 HCAPLUS
DOCUMENT NUMBER: 114:97555
TITLE: Lifetime of neutral-carrier-based liquid membranes in aqueous samples and blood and the lipophilicity of membrane components
AUTHOR(S): Dinten, Oliver; Spichiger, Ursula E.; Chaniotakis, Nicolas; Gehrig, Peter; Rusterholz, Bruno; Morf, Werner E.; Simon, Wilhelm
CORPORATE SOURCE: Dep. Org. Chem., Swiss Fed. Inst. Technol., Zurich, CH-8092, Switz.
SOURCE: Analytical Chemistry (1991), 63(6), 596-603
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: English

AB On the basis of previously reported correlations between the lipophilicity of membrane components, their partition coeff. between the membrane and the sample, and the lifetime of corresponding neutral-carrier-based sensors, the lipophilicities of ionophores and plasticizers in anal. relevant ion-selective electrodes, ISFETs, and optodes are analyzed and reported. Equations for the estn. of the lifetimes of the liq. membranes is continuous-flow systems are presented, and the exptl. detn. of the lipophilicity values by thin-layer chromatog. (TLC) is described. The required lipophilicities for the lifetimes of liq. membranes over 30 24-h days for different applications in aq. solns. as well as in blood are presented. A comparison of the exptl. results of lifetime measurements with calcd. theor. values is given. The exptl. results of the detn. of the lipophilicity by TLC are compared with the lipophilicities estd. on the basis of Hansch parameters.

IT **79748-40-6**, CIP
RL: PRP (Properties)
(lipophilicity of, as membrane component, lifetime in relation to)

L14 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:572231 HCAPLUS
DOCUMENT NUMBER: 103:172231
TITLE: Distinct behavior of .beta.-endorphin and corticotropin toward leucine aminopeptidase action
AUTHOR(S): Li, Choh Hao; Chung, David

CORPORATE SOURCE: Lab. Mol. Endocrinol., Univ. California, San Francisco, CA, 94143, USA
SOURCE: International Journal of Peptide & Protein Research (1985), 26(2), 113-17
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reactions of human .beta.-endorphin [61214-51-5], ACTH [9002-60-2], and their synthetic analogs with leucine aminopeptidase [9001-61-0] confirm previous findings that .beta.-endorphin is resistant to the aminopeptidase action whereas ACTH is not. Methionine-enkephalin [58569-55-4] is completely digested by the enzyme, but 1-17-human .beta.-endorphin [60893-02-9] is resistant. The N-terminal 7 residues in ACTH are removed readily by leucine aminopeptidase, although 7-38-human ACTH [**79748-40-6**] is not hydrolyzed by the enzyme. This contrasting behavior of .beta.-endorphin and ACTH toward leucine aminopeptidase may be related to differences in their conformational structures.
IT **79748-40-6**
RL: PRP (Properties)
(degrdn. of, by leucine aminopeptidase)

L14 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:151163 HCAPLUS
DOCUMENT NUMBER: 100:151163
TITLE: 'Dystonia'-like postural asymmetry after microinjection of ACTH N-terminal fragments but not after ACTH1-39 in rat brainstem suggests role of neuropeptide mutation in genetic movement disorder
AUTHOR(S): Jacquet, Yasuko F.
CORPORATE SOURCE: Cent. Neurochem., Rockland Res. Inst., New York, NY, 10035, USA
SOURCE: Brain Research (1984), 294(1), 144-7
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A structure-activity study showed that ACTH1-39 [11137-42-1], in contrast to its N-terminal fragments, did not have any dystonic actions, however transient or slight in rats. Thus, the folded conformation of ACTH1-39 in vivo may prevent its N-terminal region from interacting with those central nervous system sites that trigger dystonic actions. Genetically linked human dystonia may thus have originated in part as a consequence of a mutation in the processing of the ACTH mol., resulting in an aberrantly folded conformation that allows its N-terminal region to trigger the dystonic syndrome.
IT **79748-40-6**
RL: BIOL (Biological study)
(dystonia in response to, in brainstem, structure in relation to)

L14 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:97080 HCAPLUS
DOCUMENT NUMBER: 100:97080
TITLE: Acute in-vivo effects of adrenocorticotropin on plasma levels of glucagon, insulin, glucose and free fatty acids in rabbits: involvement of the alpha-adrenergic nervous system

AUTHOR(S): Knudtzon, J.
CORPORATE SOURCE: Pediatr. Res. Inst., Rikshosp., Oslo, 1, Norway
SOURCE: Journal of Endocrinology (1984), 100(3), 345-52
CODEN: JOENAK; ISSN: 0022-0795
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Injection of 8.5 nmol (1-24)-ACTH [16960-16-0] i.v. increased the plasma levels of glucagon [9007-92-5], insulin [9004-10-8], glucose, and free fatty acids in rabbits. The (1-14)-ACTH-induced hyperglucagonemia and hyperinsulinemia started 3 and 20 min after the injection, resp. Similar increases in the plasma levels of glucagon, insulin, and free fatty acids were found with 5.6 nmol (1-39)-ACTH [9002-60-2] whereas (1-4)-ACTH [19405-50-6], (4-10)-ACTH [4037-01-8], (1-10)-ACTH [2791-05-1], (11-24)-ACTH [4237-93-8], (7-38)-ACTH [**79748-40-6**], and (18-39)-ACTH [52870-23-2] (corticotropin-like intermediate lobe peptide) injected at doses of .apprx.8 nmol were inactive. Infusions with the .alpha.-adrenergic blocking drug, phentolamine, reduced the (1-24)-ACTH-induced hyperglucagonemia and hyperglycemia, and augmented the (1-24)-ACTH-induced hyperinsulinemia, which now became significant after 5 min. Infusions with the .beta.-adrenergic blocking drug, propranolol, did not diminish the (1-24)-ACTH-induced effects, but killed the rabbits after 2-4 h. Thus, the acute in vivo effects of ACTH in rabbits are modulated by the involvement of .alpha.-adrenergic receptors, which increase the plasma levels of glucagon and glucose, and delay and diminish the ACTH-induced increases in the plasma levels of insulin. The (1-24)-ACTH-induced increases in the plasma levels of free fatty acids were not influenced by the adrenergic blocking drugs.

IT **79748-40-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(fatty acids and pancreatic hormones of blood plasma response to)

L14 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1983:30201 HCAPLUS
DOCUMENT NUMBER: 98:30201
TITLE: Adrenocorticotropin-dependent particulate guanylate cyclase in rat adrenal and adrenocortical carcinoma: comparison of its properties with soluble guanylate cyclase and its relationship with ACTH-induced steroidogenesis
AUTHOR(S): Nambi, Ponnal; Aiyar, Nambi V.; Sharma, Rameshwar K.
CORPORATE SOURCE: Cent. Health Sci., Univ. Tennessee, Memphis, TN, 38163, USA
SOURCE: Archives of Biochemistry and Biophysics (1982), 217(2), 638-46
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An ACTH-dependent particulate guanylate cyclase (I) from rat adrenal gland and from rat adrenocortical carcinoma that was distinct from sol. I was previously described. Herein, the detailed kinetic and functional differences between the 2 enzymes are reported. Particulate I was stimulated by low concns. of ACTH1-39 (10-11 M) and ACTH1-24 (10-13 M). The ACTH-antagonist ACTH7-38 and

4-methyl-4-aza-5.alpha.-cholestane, compds. that competitively inhibit the steroidogenic activity of ACTH, inhibited the hormonally dependent I. In contrast, sol. I was not stimulated by ACTH. Particulate I was not stimulated by NaN3, Na nitroprusside, excess Mn2+, dithiothreitol, and N-ethylmaleimide. On the other hand, all of these agents stimulated sol. I. The half-maximal velocity of sol. I was achieved at 0.06 mM MnGTP, whereas particulate I was not saturable up to 2 mM MnGTP. Cd2+ did not affect particulate I, but inhibited sol. I. Tuftsin (10-6-10-5 M) did not stimulate the membrane I, whereas it strongly stimulated sol. I. Apparently, the adrenal particulate and sol. Is are functionally different and may also be 2 structurally independent entities.

IT **79748-40-6**
RL: BIOL (Biological study)
(guanylate cyclase of adrenal gland inhibition by, steroidogenesis in relation to)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:49:10 ON 12 AUG 2003)

L16 19 S L14
L17 0 S L16 AND ANTIBOD?
L18 12 DUP REM L16 (7 DUPLICATES REMOVED)

L18 ANSWER 1 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003345558 MEDLINE
DOCUMENT NUMBER: 22759740 PubMed ID: 12876868
TITLE: [Comparison of the intact PTH test with the total PTH test in hemodialyzed patients].
Usporedba intaktnog PTH testa s ukupnim PTH testom u hemodijaliziranih bolesnika.
AUTHOR: Pecovnik Balon Breda; Puklavec Ludvig; Hojs Radovan
CORPORATE SOURCE: Odjel za nefrologiju, Klinika za internu medicinu, Opca bolnica Maribor, Maribor, Slovenija.
SOURCE: ACTA MEDICA CROATICA, (2003) 57 (1) 69-70.
Journal code: 9208249. ISSN: 1330-0164.
PUB. COUNTRY: Croatia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Serbo-Croatian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030725
Last Updated on STN: 20030808
Entered Medline: 20030807

AB We measured PTH by intact PTH assays (iPTH) and whole PTH kit. iPTH includes 1-84 PTH (CAP) and the PTH antagonist fragment (CIP). The CAP/CIP ratio more precisely indicates the net relative actions of the agonist PTH (CAP) and the antagonist PTH fragment (CIP). The CAP/CIP ratio > 1 identifies patients with normal or high bone turnover disease, and the CAP/CIP ratio < 1 indicates patients with adynamic low bone turnover disease. Serum samples were obtained from 98 hemodialysis patients. We measured iPTH with intact PTH assay (PTH, intact Elecsys Systeme, Roche), and whole PTH with Duo PTH Assay (Scantibodies Laboratories, Santee, CA, USA), which determine human whole PTH or Cyclase Activating PTH (CAP) as well as total immunoreactive PTH (the sum of 1-84PTH and N truncated PTH fragments). **Cyclase** inactive PTH (**CIP**) is an inactive fragment 7-84 PTH and is calculated as total PTH--CAP. For the evaluation of bone turnover, the activity of serum alkaline

phosphatase (AP) was determined by the method standardized according to IFCC. The adenosine monophosphate (AMP) buffer, reagents by LEK (Boehringer), and the Technicon RA-XT device were used. Mean intact PTH = 578 +/- 767 pg/ml; CAP = 332 +/- 366 pg/ml; total PTH = 518 +/- 560 pg/ml; mean AP = 1.9 + 2.9 mukat/l; CAP/CIP ratio < 1 was found in 9 patients. Mean CAP in these patients was 71 +/- 42 pg/ml; total PTH = 172.6 +/- 104.8 and intact PTH = 150 +/- 65 pg/ml; AP = 0.8 +/- 0.2 mukat/l. It is known that patients with adynamic bone disease have intact PTH below 200 pg/ml, and our next step will be to evaluate with bone biopsy whether patients with CAP/CIP ratio actually have adynamic bone disease.

L18 ANSWER 2 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2003315837 MEDLINE
DOCUMENT NUMBER: 22729415 PubMed ID: 12845234
TITLE: An evaluation of 1-84 PTH measurement in relation to bone alkaline phosphatase and bone Gla protein in hemodialysis patients.
AUTHOR: Miwa Naoko; Nitta Kosaku; Kimata Naoki; Watanabe Yoshihiko; Suzuki Koichi; Kawashima Akira; Haga Masahiro; Watanabe Ryo-ichiro; Aoki Takanao; Akiba Takashi; Nihei Hiroshi
CORPORATE SOURCE: Department of Medicine, Kidney Center, Tokyo Women's Medical University, Shinjuku-ku, Tokyo, Japan.. miwa@kc.twmu.ac.jp
SOURCE: Nephron Clin Pract, (2003) 94 (2) c29-32. Journal code: 101159763. ISSN: 1660-2110.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030708
Last Updated on STN: 20030801
Entered Medline: 20030731

AB BACKGROUND/AIM: It has been suggested that higher levels of parathyroid hormone (PTH) are required to maintain normal bone turnover in chronic hemodialysis (HD) patients. Serum PTH levels determined by intact PTH (i-PTH) assay may overestimate the actual activity of circulating PTH in HD patients. The aim of the present study was to assess the clinical usefulness of whole PTH assay on the evaluation of bone turnover in HD patients. MATERIALS AND METHODS: We performed measurement of parameters on bone turnover in 179 HD patients (116 men, 63 women; mean age 61.0 +/- 13.1 years). Serum whole PTH levels were determined as cyclase-activating PTH (CAP) by an immunoradiometric assay, and compared with those of i-PTH. **Cyclase**-inactivating PTH (**CIP**) was calculated as (i-PTH-CAP). The correlations between serum whole PTH levels and clinical parameters such as serum levels of Ca, P, bone alkaline phosphatase (BAP), bone Gla protein (BGP), total protein (TP), albumin (Alb), urea nitrogen (SUN), and creatinine (Cr) were analyzed using multivariate analysis. RESULTS: The mean values of i-PTH and CAP were 124.1 +/- 97.4 and 86.9 +/- 71.6 pg/ml, respectively, indicating that the serum CAP levels were about 70% of i-PTH levels. The serum CAP levels significantly correlated with that of i-PTH ($r = 0.959$, $p < 0.001$). Moreover, a significant positive correlation between serum CAP levels and metabolic bone markers such as BAP ($r = 0.400$, $p < 0.01$) and BGP ($r = 0.481$, $p <$

0.01) was observed. Stepwise multivariate analysis revealed that serum levels of CAP were significantly determined by serum levels of Ca, P, Alb, and oral dosage of vitamin D (F ratio = 18.81, adjusted r(2) = 0.302). CONCLUSIONS: These data suggest that the biological activity of circulating PTH in HD patients is lower than the levels estimated by conventional i-PTH assay.

L18 ANSWER 3 OF 12 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-209227 [20] WPIDS
DOC. NO. CPI: C2003-053213
TITLE: Treating a patient having osteoporosis and is being administered cyclase activating parathyroid hormone or its analogue comprises administering a cyclase inhibiting parathyroid hormone peptide.
DERWENT CLASS: B04
INVENTOR(S): CANTOR, T L
PATENT ASSIGNEE(S): (CANT-I) CANTOR T L
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002160945	A1	20021031	(200320)*		8

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002160945	A1 Provisional	US 2000-224446P	20000810
		US 2001-928047	20010810

PRIORITY APPLN. INFO: US 2000-224446P 20000810; US 2001-928047 20010810
AN 2003-209227 [20] WPIDS
AB US2002160945 A UPAB: 20030324
NOVELTY - Treating (M1) a patient having osteoporosis comprising administering a **cyclase** inhibiting parathyroid hormone peptide (**CIP**) or its conservatively substituted variant exhibiting a parathyroid hormone (PTH) antagonist activity to reduce the occurrence of hypercalcemia or osteosarcoma in the patient resulting from the administration of CAP, is new.

DETAILED DESCRIPTION - The CIP has a sequence of 83 (PTH2-84) or 82 (PTH34-84) amino acids fully defined in the specification.

ACTIVITY - Osteopathic.

Twenty five rats had their parathyroid removed. Five rats received an intravenous injection of saline control, and serum calcium was measured and on average was lowered over time by 0.18 mg/dl. Nine rates received hPTH, and serum calcium of the HPTP rats was measured and on average was raised over time by 0.65 mg/dl. Five rats received an equimolar injection of PTH7-84 (PTH antagonist), and serum calcium of the PTH antagonist rats were measured and on average was lowered over time by 0.30 mg/dl. Six rats received pPTH and an equimolar amount of PTH antagonist PTH7-84. The serum calcium of the hPTH/PTH antagonist rats was measured, and on average remained substantially the same over time, raising only about 0.03 mg/dl. The compositions comprising the PTH antagonist was able to

prevent the substantial serum calcium increase normally associated with an administration of hPTH to rats having hypoparathyroidism, and is much more potent in its antagonist property than the previously reporter antagonist PTH3-34.

MECHANISM OF ACTION - Parathyroid hormone antagonist.

USE - (M1) is useful for treating osteoporosis (claimed).

Dwg.0/2

L18 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 2

ACCESSION NUMBER: 2002:210179 BIOSIS
DOCUMENT NUMBER: PREV200200210179
TITLE: Pituitary adenylate cyclase activating polypeptide anti-mitogenic signaling in cerebral cortical progenitors is regulated by p57Kip2-dependent CDK2 activity.
AUTHOR(S): Carey, Rebecca G.; Li, Baogang; DiCicco-Bloom, Emanuel (1)
CORPORATE SOURCE: (1) 675 Hoes Lane, Room 338 CABM, Piscataway, NJ, 08854: diciccem@umdnj.edu USA
SOURCE: Journal of Neuroscience, (March 1, 2002) Vol. 22, No. 5, pp. 1583-1591. http://www.jneurosci.org/. print. ISSN: 0270-6474.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Generation of distinct cell types and numbers in developing cerebral cortex is subject to regulation by extracellular factors that positively or negatively control precursor proliferation. Although signals stimulating proliferation are well described, factors halting cell cycle progression are less well defined. At the molecular level, production and association of cyclins, cyclin-dependent kinases (CDKs), and CDK inhibitors (CKIs) regulate cycle progression. We now report that the endogenous peptide, pituitary adenylate **cyclase** activating polypeptide (PACAP), negatively regulates the cell cycle by inhibiting p57Kip2-dependent CDK2 activity in embryonic cortex. Protein levels of CDK2 and members of the **CIP**/KIP family of CKIs (p27Kip1, p57Kip2) were detected in developing rat cortex from embryonic day 13.5 through postnatal day 2. With advancing development, CDK2 protein levels decreased, whereas CKI expression increased, suggesting that stimulatory and inhibitory cycle proteins control cell cycle exit. Using a well defined, nonsynchronized, 8 hr precursor culture, PACAP decreased the fraction of cells crossing the G1/S boundary, inhibiting DNA synthesis by 35%. CDK2 kinase activity was inhibited 75% by PACAP, whereas kinase protein and its regulatory cyclin E subunit were unaffected. Moreover, decreased kinase activity was accompanied by a twofold increase in levels of p57Kip2 protein, but not p21Cip1 or p27Kip1, suggesting that p57Kip2 mediates PACAP anti-mitogenic effects. Indeed, immunoprecipitation of CDK2 complex revealed increased p57Kip2 association with the kinase and concomitant reduction in free inhibitor after PACAP exposure, suggesting that p57Kip2 interactions directly regulate CDK2 activity. These observations establish a mechanism whereby anti-mitogenic signals actively induce cell cycle withdrawal in developing cortex.

L18 ANSWER 5 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2002608011 MEDLINE

DOCUMENT NUMBER: 22253739 PubMed ID: 12369051
TITLE: [Intact whole bioactive parathormone: problems arising from comparing different methods]. Paratormone intatto intero bioattivo: le problematiche emergenti dal confronto.
AUTHOR: Marangella M; Migliardi M; Dutto F; Mengozzi G; Marranca D; Bagnis C; Berutti S; Gallone G; Aimo G; Ramello A; Fonzo D
CORPORATE SOURCE: UU.OO. Nefrologia Dialisi e Centro Calcolosi Renale, Italy.. mmarangella@mauriziano.it
SOURCE: G Ital Nefrol, (2002 Jul-Aug) 19 (4) 467-75. Journal code: 9426434. ISSN: 0393-5590.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (EVALUATION STUDIES) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021008 Last Updated on STN: 20021218 Entered Medline: 20021216

AB BACKGROUND: Parathyroid hormone (PTH) has important applications in the nephrological clinical practice. Because assays of Intact PTH (I-PTH) are liable to interferences by N-truncated fragments, a novel method for whole-(1-84) PTH has been proposed. This study is aimed at comparing the latter with some of the previous I-PTH assays. For each method the results are referred to pertinent markers of mineral metabolism. METHODS: We enrolled 171 subjects, including 56 healthy controls (C), 65 calcium stone- formers (CaSF), 40 haemodialysis patients (HD), 10 with primary hyperparathyroidism (PHP). On blood samples we measured: I-PTH by four methods (N-Tact, Advantage, Elecsys, Scantibodies), whole-(1-84) PTH, defined as CAP (Cyclase Activating PTH), total and ionised calcium, phosphate, vitamin D, osteocalcin and Crosslaps. The difference between I-PTH and CAP Scantibodies is defined as **CIP** (**Cyclase** Inhibiting PTH). RESULTS: Despite relating to each other ($r>0.97$) PTH values varied remarkably among methods. For all methods, the reference intervals differed from those provided by the producer. Assuming these new ranges, 10 CaSF had over-range values not always associated with abnormalities of mineral metabolism. One of the PHP patients was normal for I-PTH with 2/4 methods. In HD the differences among methods were even greater, there were inverse ($p<0.05$) and direct ($p<0.001$) relationships with ionised calcium and osteocalcin-crosslaps, respectively. The CAP/CIP ratio was lower in low bone turnover patients, but the two subgroups widely overlapped. CONCLUSIONS: This study indicates that the reliability of I-PTH assays is still unsatisfactory, and none of the four methods emerged as the best. Assay for CAP only improves diagnostic efficiency, whereas the CAP/CIP ratio does not exhibit powerful discriminating capacity. Our suggestion is that each Centre should establish its own reference ranges. PTH assay should always be coupled with measurements of other markers of mineral metabolism as well as renal function.

L18 ANSWER 6 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:629285 BIOSIS
DOCUMENT NUMBER: PREV200200629285

TITLE: Influence of sevelamer hydrochloride on plasma concentration of **cyclase** activating (CAP) and inhibiting (**CIP**) fragments respectively of parathyroid hormone in haemodialysis (HD) uraemic patients.
AUTHOR(S): Piecha, G. (1); Chudek, J. (1); Kokot, F. (1); Wiecek, A. (1)
CORPORATE SOURCE: (1) Dept. of Nephrology, Endocrinology and Metabolic Diseases, Silesian University School of Medicine, Katowice Poland
SOURCE: Nephrology Dialysis Transplantation, (2002) Vol. 17, No. Abstracts Supplement 1, pp. 69. print.
Meeting Info.: XXXIX Congress of the European Renal Association and the European Dialysis and Transplant Association Copenhagen, Denmark July 14-17, 2002 European Dialysis and Transplant Association
. ISSN: 0931-0509.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:629161 BIOSIS
DOCUMENT NUMBER: PREV200200629161
TITLE: Intact PTH and 7-84 PTH fragments in hemodialysis patients.
AUTHOR(S): Malberti, F. (1); Bufano, P. (1); Pecchini, P. (1); Ravani, P. (1); Gnocchi, E. (1)
CORPORATE SOURCE: (1) Divisione di Nefrologia e Medicina Nucleare, Cremona Italy
SOURCE: Nephrology Dialysis Transplantation, (2002) Vol. 17, No. Abstracts Supplement 1, pp. 31-32. print.
Meeting Info.: XXXIX Congress of the European Renal Association and the European Dialysis and Transplant Association Copenhagen, Denmark July 14-17, 2002 European Dialysis and Transplant Association
. ISSN: 0931-0509.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:3900 BIOSIS
DOCUMENT NUMBER: PREV200200003900
TITLE: PACAP negatively regulates precursor proliferation through p57KIP2 inhibition of CDK2 in developing cerebral cortex.
AUTHOR(S): Suh, J. (1); Carey, R. (1); DiCicco-Bloom, E. (1)
CORPORATE SOURCE: (1) Dept Neuroscience and Cell Biology, UMDNJ-Robert Wood Johnson Medical School, Piscataway, NJ USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2374. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB During generation of the multi-layered cerebral cortex, cellular laminar fate is strictly determined by the time when proliferative precursors exit the cell cycle, though regulatory signaling cascades are just being defined. Previously, we found that the endogenous peptide, pituitary adenylate **cyclase**-activating polypeptide (PACAP), inhibited cortical proliferation and induced neuronal differentiation in vitro. Moreover, transuterine intraventricular injection of PACAP inhibited mitosis in the ventricular zone without inducing apoptosis, whereas blocking endogenous peptide signaling stimulated DNA synthesis, suggesting that PACAP tonically restrains ongoing proliferation in the embryo. To begin defining molecular mechanisms, we focused on cyclin-dependent kinase (CDK) inhibitors, specifically members of the **CIP**/KIP family (p21, p27, p57), which prevent cell cycle progression from G1 to S-phase by blocking the activity of CDK2/cyclin E complexes. In 8hr cultures, in which PACAP inhibited DNA synthesis by 26%, the peptide induced a 3-fold increase in levels of p57 protein, without affecting p27 or p21. Further, PACAP treatment elicited transfer of p57 from the cytosol to CDK2/cyclin E complexes, which association reduced CDK2 kinase activity by 75%. Finally, the mitotic inhibitory role of p57 in cortical precursors was extended to the embryo, in which PACAP ICV injection increased p57 protein at 4hr, suggesting that p57 plays a central role in anti-mitogenic signaling during brain ontogeny.

L18 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:399969 BIOSIS
DOCUMENT NUMBER: PREV200100399969
TITLE: Duo PTH assay kit for the determination of human PTH1R agonist/antagonist ratio in patients with uremia.
AUTHOR(S): Cantor, T. (1); Scheibel, S. (1); Gao, P. (1); Lepage, R.; Cook, D. (1); D'Amour, P.
CORPORATE SOURCE: (1) Scantibodies Laboratory, Inc., Santee, CA USA
SOURCE: Nephrology Dialysis Transplantation, (June, 2001) Vol. 16, No. 6, pp. A9. print.
Meeting Info.: Annual Congress of the European Renal Association and the European Dialysis and Transplant Association Vienna, Austria June 24-27, 2001
ISSN: 0931-0509.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L18 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 3

ACCESSION NUMBER: 1999:442815 BIOSIS
DOCUMENT NUMBER: PREV199900442815
TITLE: Gastric inhibitory polypeptide stimulates glucocorticoid secretion in rats, acting through specific receptors coupled with the adenylate cyclase-dependent signaling pathway.
AUTHOR(S): Mazzocchi, Giuseppina; Rebuffat, Piera; Meneghelli, Virgilio; Malendowicz, Ludwik K.; Tortorella, Cinzia; Gottardo, Giuseppe; Nussdorfer, Gastone G. (1)
CORPORATE SOURCE: (1) Department of Human Anatomy and Physiology, Section of Anatomy, University of Padua, Via Gabelli

65, I-35121, Padua Italy
SOURCE: Peptides (New York), (1999) Vol. 20, No. 5, pp. 589-594.
ISSN: 0196-9781.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Gastric inhibitory polypeptide (GIP) is a 42-amino acid peptide, belonging to the VIP-secretin-glucagon superfamily, some members of this group are able to regulate adrenocortical function. GIP-receptor mRNA has been detected in the rat adrenal cortex, but investigations on the effect of GIP on steroid-hormone secretion in this species are lacking. Hence, we have investigated the distribution of GIP binding sites in the rat adrenal gland and the effect of their activation in vivo and in vitro. Autoradiography evidenced abundant (125I)GIP binding sites exclusively in the inner adrenocortical layers, and the computer-assisted densitometric analysis of autoradiograms demonstrated that binding was displaced by cold GIP, but not by either ACTH or the selective ACTH-receptor antagonist corticotropin-inhibiting peptide (**CIP**). The intraperitoneal (IP) injection of GIP dose-dependently raised corticosterone, but not aldosterone plasma concentration: the maximal effective dose (10 nmol/rat)elicited a twofold increase. GIP did not affect aldosterone and cyclic-AMP release by dispersed zona glomerulosa cells. In contrast, GIP enhanced basal corticosterone secretion and cyclic-AMP release by dispersed inner adrenocortical cells in a concentration-dependent manner, and the maximal effective concentration (10-7 M) evoked 1.5- and 2.4-fold rises in corticosterone and cyclic-AMP production, respectively. GIP (10-7 M) did not display any additive or potentiating effect on corticosterone and cyclic-AMP responses to submaximal or maximal effective concentrations of ACTH. The corticosterone secretagogue action of 10-7 M GIP was abolished by the protein kinase A (PKA) inhibitor H-89 (10-5 M), and unaffected by **CIP** (10-6 M). Collectively, these findings indicate that GIP exerts a moderate but statistically significant stimulatory effect on basal glucocorticoid secretion in rats, acting through specific receptors coupled with the adenylate **cyclase**/PKA-dependent signaling pathway.

L18 ANSWER 11 OF 12 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1998:701387 SCISEARCH
THE GENUINE ARTICLE: 118HA
TITLE: Effect of cholesterol/phospholipid ratio on stimulatory GTP-binding protein function
AUTHOR: Bai L; Huang Y G (Reprint)
CORPORATE SOURCE: ACAD SINICA, INST BIOPHYS, NATL LAB BIOMACROMOL, BEIJING 100101, PEOPLES R CHINA (Reprint); ACAD SINICA, INST BIOPHYS, NATL LAB BIOMACROMOL, BEIJING 100101, PEOPLES R CHINA
COUNTRY OF AUTHOR: PEOPLES R CHINA
SOURCE: BIOCHEMISTRY AND MOLECULAR BIOLOGY INTERNATIONAL, (SEP 1998) Vol. 45, No. 6, pp. 1155-1162.
Publisher: ACADEMIC PRESS AUST, LOCKED BAG 16, MARRICKVILLE NSW 2204, AUSTRALIA.
ISSN: 1039-9712.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English

REFERENCE COUNT: 27
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The effect of different cholesterol/phospholipid (C/P) ratios on the coupling function between stimulatory GTP-binding protein(Gs) and adenylyl **cyclase** (AC) in proteoliposomes, and its relationship to the conformational change of Gs were investigated. The results showed that Gs activities of both binding GTP gamma S and stimulating adenylyl **cyclase** were the highest in proteoliposomes with a proper content of cholesterol similar to physiological situation while the lowest with. higher cholesterol content similar to pathological situation. In addition, the conformational change of Gs in proteoliposomes was also detected by steady-state and nanosecond time-resolved fluorescence using acrylodan as a probe. It is suggested that a proper **CIP** ratio similar to physiological situation regulates the function of Gs by inducing a change in the physical state of lipid bilayer, which would favor the formation of a suitable conformation of Gs with higher activities of both binding GTP and stimulating adenylyl **cyclase**. But if C/P ratio is higher, such as in pathological situation, this is unfavorable for motion of Gs in membrane, which results in inhibition of Gs function significantly.

L18 ANSWER 12 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 4

ACCESSION NUMBER: 1999:87560 BIOSIS
DOCUMENT NUMBER: PREV199900087560
TITLE: The possible involvement of pancreatic polypeptide in the paracrine regulation of human and rat adrenal cortex.
AUTHOR(S): Nussdorfer, G. G. (1); Mazzocchi, G. (1); Malendowicz, L. K.
CORPORATE SOURCE: (1) Dep. Anat., Univ. Padua, Padua Italy
SOURCE: Endocrine Research, (Aug.-Nov., 1998) Vol. 24, No. 3-4, pp. 695-702.
ISSN: 0743-5800.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Pancreatic polypeptide (PP) is a member of a family of 36-amino acid brain-gut peptides, including neuropeptide Y (NPY) and polypeptide YY (PYY) and acting through many subtypes of Y receptors belonging to the superfamily of the G protein-coupled receptors. PP was found to increase both glucocorticoid and cyclic-AMP production by dispersed rat and human adrenocortical cells in a concentration-dependent manner. Minimal and maximal effective concentrations were 10-10 and 10-8 M, respectively. The glucocorticoid secretagogue effect of 10-8 M PP was blocked by the protein kinase A (PKA) unhibitor H-89, but not by the ACTH-receptor antagonist corticotropin-inhibiting peptide (**CIP**). Autoradiography showed the presence of (125I)PP binding sites in the inner zones of rat and human adrenal cortex, which were not displaced by NPY, PYY, ACTH or **CIP**. Sizable amounts of PP-immunoreactivity were detected in the medulla of both rat and human adrenals (about 50-100 fmol/mg); this content may give rise, upon submaximal stimulation of PP release, to local intraadrenal concentrations of about 10-8/10-7 M. Collectively, these findings allow us to draw the following conclusions: (i) PP stimulates glucocorticoid secretion, acting through specific receptors coupled with the adenylate **cyclase**/PKA-dependent signaling

pathway; and (ii) PP could be included in that group of regulatory peptides, contained in adrenal medulla, which are able to control the secretory function of the cortex acting in a paracrine manner.

FILE 'HOME' ENTERED AT 15:50:13 ON 12 AUG 2003

** May contain prev. viewed citations

(FILE 'REGISTRY' ENTERED AT 11:30:01 ON 13 AUG 2003)
E PARATHYROID HORMONE/CN
L2 12 S E3-E13
E PARATHORMONE/CN
L3 10 S E3 OR E4 OR E6 OR E8-E10 OR E13 OR E15 OR E16
L4 20 S L2 OR L3

L5 747 S CYCLASE?/CN

FILE 'HCAPLUS' ENTERED AT 11:32:12 ON 13 AUG 2003
L2 12 SEA FILE=REGISTRY ABB=ON PLU=ON ("PARATHYROID HORMONE"/CN OR "PARATHYROID HORMONE (BOVINE)"/CN OR "PARATHYROID HORMONE (HUMAN)"/CN OR "PARATHYROID HORMONE (HUMAN) FUSION PROTEIN WITH APELIN 36 (HUMAN)"/CN OR "PARATHYROID HORMONE (HUMAN) FUSION PROTEIN WITH G PROTEIN-COUPLED RECEPTOR 8 GPR8 LIGAND (HUMAN)"/CN OR "PARATHYROID HORMONE (HUMAN) FUSION PROTEIN WITH G PROTEIN-COUPLED RECEPTOR ZAQ LIGAND (HUMAN)"/CN OR "PARATHYROID HORMONE (MACAQUE)"/CN OR "PARATHYROID HORMONE (PORCINE)"/CN OR "PARATHYROID HORMONE (RAT)"/CN OR "PARATHYROID HORMONE (RATTUS NORVEGICUS 115-AMINO ACID)"/CN OR "PARATHYROID HORMONE (SYNTHETIC CLONE 4PTH)"/CN)
L3 10 SEA FILE=REGISTRY ABB=ON PLU=ON PARATHORMONE/CN OR "PARATHORMONE (16-ASPARTIC ACID) (HUMAN)"/CN OR "PARATHORMONE (29-HISTIDINE) (HUMAN)"/CN OR ("PARATHORMONE (35-CYSTEINE) (HUMAN)"/CN OR "PARATHORMONE (37-THREONINE) (HUMAN)"/CN OR "PARATHORMONE (57-ASPARTIC ACID) (HUMAN)"/CN) OR "PARATHORMONE (8-CYSTEINE) (HUMAN)"/CN OR "PARATHORMONE (CANIS FAMILIARIS)"/CN OR "PARATHORMONE (CATTLE)"/CN
L4 20 SEA FILE=REGISTRY ABB=ON PLU=ON L2 OR L3
L5 747 SEA FILE=REGISTRY ABB=ON PLU=ON CYCLASE?/CN
L6 44184 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 OR CYCLASE
L7 18635 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 OR (PARATHYROID? OR PARA THYROID?)(W)HORMONE OR PARATHORMONE OR PTH
L8 1285 SEA FILE=HCAPLUS ABB=ON PLU=ON L6(L)L7
L9 61 SEA FILE=HCAPLUS ABB=ON PLU=ON L8(L)INACTIV?
L10 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND ANTIBOD?

L10 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:150478 HCAPLUS
DOCUMENT NUMBER: 138:199234
TITLE: Methods for monitoring and guiding therapeutic suppression of parathyroid hormone in renal patients having secondary hyperparathyroidism
INVENTOR(S): Cantor, Thomas L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6524788	B1	20030225	US 2001-2818	20011102
WO 2003039572	A1	20030515	WO 2002-US35516	20021104

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-2818 A 20011102
US 2002-286465 A 20021101

AB The present invention relates to novel methods for monitoring and guiding therapeutic suppression of **parathyroid hormone** in renal patients having secondary hyperparathyroidism. One dets. and monitors the level of **cyclase** activating **parathyroid hormone** and **cyclase inactive parathyroid hormone** in the renal patient. The **parathyroid hormone** suppressing therapeutic is administered to the patient so as to minimize the level of **cyclase inactive parathyroid hormone.**

IT **9002-64-6DP, Parathyroid hormone,** **cyclase** activating PTH1-84, **cyclase inactive** PTH2-84 and **cyclase inactive** PTH34-84
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for monitoring and guiding therapeutic suppression of **parathyroid hormone** in renal patients having secondary hyperparathyroidism)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:507044 HCAPLUS
DOCUMENT NUMBER: 115:107044
TITLE: Altered differentiation of limb bud cells by transforming growth factors-.beta. isolated from bone matrix and from platelets
AUTHOR(S): Schoenfeld, Hans Joachim; Poeschl, Bernd; Wessner, Bruno; Kistler, Andreas
CORPORATE SOURCE: Cent. Res. Units, F. Hoffmann-La Roche Ltd., Basel, CH-4002, Switz.
SOURCE: Bone and Mineral (1991), 13(3), 171-89
CODEN: BOMIET; ISSN: 0169-6009
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A crude ext. of demineralized bone matrix caused an altered differentiation of limb bud cells which was seen within 5 days in culture. Using this bioassay system 2 factors were purified to homogeneity and were found, according to their N-terminal sequences, to correspond to transforming growth factor-B1 (TGF-.beta.1) and TGF-.beta.2 isolated from platelets. Biochem. analyses and biol.

studies (mol. mass detn., **inactivation** by reducing agents and proteases, **antibody** neutralization, competitive binding to TGF-.beta. receptors, and influence on protein expression) provided addnl. evidence that the 2 proteins isolated from demineralized bone matrix were apparently identical to TGF-.beta.1 and TGF-.beta.2. Proteoglycan content, alk. phosphatase activity, and response of the cells to **parathyroid hormone**-stimulated adenylate **cyclase** were quant. changed by the factors. Culturing limb bud cells on polycarbonate membranes resulted in a rapid and extensive growth and differentiation of the cells to palpable tissue pieces. Relative to controls distinct cell and tissue morphol. was obsd. macroscopically and in histol. sections of these tissue pieces.

L10 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:573998 HCAPLUS
DOCUMENT NUMBER: 89:173998
TITLE: Evidence for glomerular receptors for parathyroid hormone
AUTHOR(S): Sraer, J.; Sraer, J. D.; Chansel, D.; Jueppner, H.; Hesch, R. D.; Ardaillou, R.
CORPORATE SOURCE: Inst. Natl. Sante Rech. Med., Tenon Hosp., Paris, Fr.
SOURCE: American Journal of Physiology (1978), 235(2), F96-F103
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rat renal glomerular receptors for **parathyroid hormone (PTH)** [**9002-64-6**] were demonstrated by 2 techniques; direct binding studies of 3H-labeled (1-34)-human **parathyroid hormone** (I) [52232-67-4] and an indirect approach using 125I-labeled specific **antibodies** directed against either I or (1-84)-bovine **PTH**. Binding equil. was reached both at increasing incubation times and increasing **PTH** concns. I-3H binding was inhibited by unlabeled hormone and its analogs, but by neither unrelated peptides nor **inactivated PTH**. Addn. of an excess of unlabeled I at equil. produced release of the tritiated hormone from its receptors. I-3H did not bind to nontarget tissues, but there was a close relation between I-3H binding and adenylate **cyclase** [**9012-42-4**] stimulation by this tracer, with both processes displaying similar KD values close to 10-7 M. The peptides which competed with I-3H for its binding sites were potent stimulators of adenylate **cyclase** activity, whereas those without effect on **PTH** binding were also **inactive** on this enzyme. Nonspecific binding represented 20-33% of total binding. Binding was pH and temp. dependent, max. binding being obsd. at pH 7.3 and 10.degree.. Binding also increased with Ca concn. in the range 0.01-1 mM. The effect of **PTH** on glomerular filtration rate may involve a direct interaction with **PTH** binding sites in the renal glomeruli.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:33:34 ON 13 AUG 2003)
L11 7 S L10
L12 4 DUP REM L11 (3 DUPLICATES REMOVED)

L12 ANSWER 1 OF 4 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 94:252375 SCISEARCH
THE GENUINE ARTICLE: NG467
TITLE: INACTIVATION BY PLASMA MAY BE RESPONSIBLE FOR LACK OF EFFICACY OF PARATHYROID-HORMONE ANTAGONISTS IN HYPERCALCEMIA OF MALIGNANCY
AUTHOR: KUKREJA S C (Reprint); DANZA J J; WIMBISCUS S A; FISHER J E; MCKEE R L; CAULFIELD M P; ROSENBLATT M
CORPORATE SOURCE: W SIDE VET ADM MED CTR, ENDOCRINOL SECT MP115, 820 S DAMEN AVE, CHICAGO, IL, 60612 (Reprint); MERCK SHARP & DOHME LTD, RES LABS, W POINT, PA, 19486; NICHOLS INST, SAN JUAN CAPISTRANO, CA, 92690; BETH ISRAEL HOSP, BOSTON, MA, 02215
COUNTRY OF AUTHOR: USA
SOURCE: ENDOCRINOLOGY, (MAY 1994) Vol. 134, No. 5, pp. 2184-2188.
ISSN: 0013-7227.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 21
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **PTH**-related protein (PTHrP) has been shown to be a major factor responsible for hypercalcemia of malignancy. PTHrP acts via the **PTH**/ PTHrP receptor, and therefore, **PTH** antagonists might be expected to reverse the hypercalcemia in malignancy. In the present studies, the **PTH** antagonists .cents.Tyr(34)|bovine (b) **PTH**-(7-34)NH2, .cents.D-Trp(12),Tyr(34)|-bPTH-(7-34)NH2, or PTHrP-(7-34)NH2, were administered to hypercalcemic athymic nude mice bearing a human squamous cell carcinoma of the lung in 60- to 500-fold molar excess of a dose of PTHrP-(1-34) known to produce hypercalcemia. The antagonists had no significant effect on serum calcium levels. In an adenylyl **cyclase** assay using the ROS 17/2.8 cells, a potent **PTH** antagonist, .cents.Leu(11),D-Trp(12)|PTHrP-(7-34)NH2 was rapidly **inactivated** in the presence of rat or human plasma. This **inactivation** by plasma was not blocked by common inhibitors of proteolysis (aprotinin, soybean trypsin inhibitor, and leupeptin). Preliminary studies demonstrated that **inactivation** of the PTHrP antagonist was caused by a plasma component with an apparent mol wt of 230,000 daltons. The knowledge of the structure of the **PTH**/PTHrP receptor combined with the identification of a hormone-**inactivating** plasma factor should facilitate the design of **PTH**-antagonists that are effective in vivo.

L12 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 91322561 MEDLINE
DOCUMENT NUMBER: 91322561 PubMed ID: 1650618
TITLE: Altered differentiation of limb bud cells by transforming growth factors-beta isolated from bone matrix and from platelets.
AUTHOR: Schonfeld H J; Poschl B; Wessner B; Kistler A
CORPORATE SOURCE: Central Research Unit, F. Hoffmann-La Roche Ltd., Basle, Switzerland.
SOURCE: BONE AND MINERAL, (1991 Jun) 13 (3) 171-89.
Journal code: 8610542. ISSN: 0169-6009.
PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19910929
Last Updated on STN: 19910929
Entered Medline: 19910912

AB A crude extract of demineralized bone matrix caused an altered differentiation of limb bud cells which was seen within 5 days in culture. Using this bioassay system we purified two factors to homogeneity and found that according to their N-terminal sequences they corresponded to TGF-beta 1 and TGF-beta 2 isolated from platelets. Biochemical analyses and biological studies (molecular mass determination, **inactivation** by reducing agents and proteases, **antibody** neutralization, competitive binding to TGF-beta receptors and influence on protein expression) provided additional evidence that the two proteins isolated from demineralized bone matrix were apparently identical to TGF-beta 1 and TGF-beta 2. Proteoglycan content, alkaline phosphatase activity and response of the cells to **PTH** stimulated adenylate **cyclase** were quantitatively changed by the factors. Culturing limb bud cells on polycarbonate membranes resulted in a rapid and extensive growth and differentiation of the cells to palpable tissue pieces. Relative to controls distinct cell and tissue morphology was observed macroscopically and in histological sections of these tissue pieces.

L12 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1979:154597 BIOSIS
DOCUMENT NUMBER: BA67:34597
TITLE: EVIDENCE FOR GLOMERULAR RECEPTORS FOR PARATHYROID HORMONE.
AUTHOR(S): SRAER J; SRAER J D; CHANSEL D; JUEPPNER H; HESCH R D; ARDAILLOU R
CORPORATE SOURCE: RES. UNIT 64, INST. NATL. SANTE RECH. MED., TENON HOSP., 75020 PARIS, FR.
SOURCE: AM J PHYSIOL, (1978) 235 (2), F96-F103.
CODEN: AJPHAP. ISSN: 0002-9513.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Glomerular receptors for **parathyroid hormone** (**PTH**) were demonstrated by 2 techniques: direct binding studies of 3H-labeled 1-34 human **parathyroid hormone** (hPTH) and an indirect approach using 125I-labeled specific **antibodies** directed against either 1-34 human or 1-84 bovine **PTH**. Specificity of binding relies on the following: binding equilibrium was reached both at increasing incubation times and increasing **PTH** concentrations; 1-34 [3H]hPTH binding was inhibited by unlabeled hormone and its analogs but by neither unrelated peptides nor **inactivated PTH**; addition of an excess of unlabeled 1-34 hPTH at equilibrium produced release of the tritiated hormone from its receptors; 1-34 [3H]hPTH did not bind to nontarget tissues; there was a close relationship between 1-34 [3H]hPTH binding and adenylate **cyclase** stimulation by this tracer, both processes displaying similar KD values close to 10-7 M; the peptides which compete with 1-34 [3H]hPTH for its binding sites were potent

stimulators of adenylate **cyclase**, whereas those without effect on **PTH** binding were also **inactive** on this enzyme. Nonspecific binding represented 20-33% of total binding. Binding was pH and temperature dependent, maximum binding being observed at pH 7.3 and 10.degree. C. Binding also increased with Ca concentration in the range 0.01-1 mM. The degradation rate of 1-34 [3H]hPTH was slow and allowed binding at equilibrium to be studied without correcting hormone concentrations. The effect of **PTH** on glomerular filtration rate may involve a direct interaction with **PTH** binding sites in the renal glomeruli.

L12 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 79160294 EMBASE
DOCUMENT NUMBER: 1979160294
TITLE: Evidence for glomerular receptors for parathyroid hormone.
AUTHOR: Sraer J.; Sraer J.D.; Chansel D.; et al.
CORPORATE SOURCE: Inst. Nat. Sante Rech. Med. Res. Unit 64, Tenon Hosp., Paris 75020, France
SOURCE: American Journal of Physiology - Renal Fluid and Electrolyte Physiology, (1978) 4/2 (F96-F103). CODEN: AJPFDM
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
002 Physiology
LANGUAGE: English
AB Glomerular receptors for **parathyroid hormone** (**PTH**) were demonstrated by two techniques: direct binding studies of 3H-labeled 1-34 human **parathyroid hormone** (hPTH) and an indirect approach using 125I-labeled specific **antibodies** directed against either 1-34 human or 1-84 bovine **PTH**. Specificity of binding relies on the following: binding equilibrium was reached both at increasing incubation times and increasing **PTH** concentrations; 1-34 [3H]hPTH binding was inhibited by unlabeled hormone and its analogues but by neither unrelated peptides nor **inactivated PTH**; addition of an excess of unlabeled 1-34 hPTH at equilibrium produced release of the tritiated hormone from its receptors; 1-34 [3H]hPTH did not bind to nontarget tissues; there was a close relationship between 1-34 [3H]hPTH binding and adenylate **cyclase** stimulation by this tracer, both processes displaying similar K(D) values close to 10-7 M; the peptides which compete with 1-34 [3H]hPTH for its binding sites were potent stimulators of adenylate **cyclase**, whereas those without effect on **PTH** binding were also **inactive** on this enzyme. Nonspecific binding represented 20-33% of total binding. Binding was pH and temperature dependent, maximum binding being observed at pH 7.3 and 10.degree.C. Binding also increased with calcium concentration in the range 0.01-1 mM. The degradation rate of 1-34 [3H]hPTH was slow and allowed binding at equilibrium to be studied without correcting hormone concentrations. The present study suggests that the effect of **PTH** on glomerular filtration rate may involve a direct interaction with **PTH** binding sites in the renal glomeruli.

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